COLLABORATIVE PRACTICE AGREEMENT
WITH PHYSICIANS AND REGISTERED PROFESSIONAL NURSES
(For practices limited to administration and dispensing medication during a mass prophylaxis event)

THIS COLLABORATIVE PRACTICE AGREEMENT (hereinafter "Agreement") is entered into by and between_____, a physician licensed to practice medicine in the State of Missouri (hereinafter "Physician") and Registered Professional Nurses (hereinafter "RNs") employed by, or serving as volunteers for, the _____ (hereinafter "Agency"), and shall be effective as of _____, 200_.

The purpose of this Agreement is to delegate to the RNs authority to perform certain medical acts. This Agreement only applies to delegated medical acts and those nursing acts requiring physician orders and not to RN's independent practice of nursing.

Section 1. Delegation, Scope of Collaborative Practice, Methods of Treatment

1.1 Physician has considered RNs' skill, training, education, and competence and has determined that,
(a) the responsibilities delegated herein are within the scope of practice of the RN and are consistent with RN's skills, training, education, and competence; and
(b) the methods of treatment and the authority to administer and dispense drugs and medications delegated to RN herein are consistent with both the Physician's and RN's skill, training, education and competence, and within the scope of practice of both.

1.2 Physician hereby delegates to RNs the authority to administer and dispense drugs pursuant to this Agreement and Exhibit A attached hereto. Exhibit A, which is jointly agreed upon protocols or standing orders, describes a specific sequence of orders, steps or procedures to be followed by the RNs providing health care services in specific mass prophylaxis clinic situations. This delegation authorizes the RNs to provide health care services to individuals who have been exposed to a known or potentially harmful biological agent.

1.3 The methods of treatment and the authority to administer and dispense drugs delegated to the RNs may not be further delegated by the RNs to any other person except the RNs may communicate prescription drug orders of Physician or an advanced practice nurse to a pharmacist.

1.4 The authority to administer and dispense drugs delegated to the RNs pursuant to Section 1.2 of this Agreement is subject to the following conditions:

(a) RNs shall not, under any circumstances, prescribe drugs or medications. The administering or dispensing of controlled substances by the RNs under this Agreement shall be accomplished only under the direction and supervision of Physician, and shall only occur on a case-by-case determination of the patient's needs following verbal consultation and order between Physician and the RN.
(b) As a publicly funded clinic in a community health setting that dispenses medications free of charge, RNs may dispense the recommended regime of antibiotic prophylactic treatment.
(c) All prescription container-labeling requirements outlined in Section 338.059 R.S.Mo. shall be followed.
(d) Retrievable dispensing logs shall be maintained for all prescription drugs dispensed and shall include all information required by state and federal statutes, rules, or regulations.

Section 2. Geographic Restrictions

2.1 Physician's practice is located at _____. The RNs will practice at designated dispensing sites located in _____ (county or counties). Physician(s) and RNs agree that the distance between these locations will not create an impediment to effective collaboration in the delivery of mass prophylactic services.

Section 3. Review of Services

3.1 During the mass prophylaxis clinics the Physician shall at all times be immediately available for consultation to the RNs, either personally or via telecommunications.

3.2 Physician shall review the work, records, and practice of health care delivered pursuant to this Agreement at least two (2) weeks of delivery of service. Review shall be documented and signed by the physician.

3.3 In the case of collaborating physicians, registered professional nurses, or advanced practice nurses practicing in association with public health clinics that provide population-based health services related to epidemiologic investigations and related treatment. Methods of treatment and review of services shall occur as set forth in the collaborative practice arrangement. If the services provided in such settings include diagnosis and initiation of treatment of disease or injury not related to population-based health services, then the provisions of sections 2, 3, and 4 of the collaborative practice act shall apply (see attached copy).
*AUTHORITY: sections 334.104.3, RSMo Supp. 2002, and 334.125 and 335.036, RSMo2000. * Original rule filed Jan. 29, 1996, effective Sept. 30, 1996. Amended: Filed April 1, 1998, effective Oct 30, 1998. Amended: Filed Oct 30, 2002, effective June 30, 2003. * Original authority: 334.104.3, RSM0 1993 amended 2002; 334.125, RSMo 1959, amended 1993, 1995; and 335.036 RSMo 1975, amended, 1981, 1985, 1993, 1995, and 1999.*

Section 4. Miscellaneous Provisions

4.1 Physician and the Agency agree to maintain copies of this Agreement, any and all amendments, all protocols and standing orders and amendments and modifications thereto and any notice of termination of this Agreement for a minimum of eight (8) years after termination of this Agreement.

4.2 The Agency agrees to maintain records of individuals receiving prophylaxis, or referral to a physician or health facility, according to the agency's current policy and procedure for record retention.

4.2 The process and documentation of review of health care services described in Sections 1.4(a) and 3.2 above shall be on file and maintained at the Agency.

4.3 Attached hereto and incorporated herein by reference as Exhibit B are guidelines for consultation and referral to Physician or a designated health facility for services or emergency care that is beyond the education, training, competence or scope of practice of the RNs.

4.4 Physician hereby designates _____(M.D. or D.O.) to consult, direct or supervise RNs in the event Physician is unable due to temporary illness, injury, or absence.

4.5 This Agreement and all Exhibits and attachments shall be reviewed and revised as needed upon the mutual written consent of Agency, RN agent, and Physician.

4.6 This Agreement may be terminated at any time by Physician and/or upon agreement of the Agency and RN agent upon _____ day's written notice to the other.

By signing this Agreement, Physician and the RN agent for the Agency, represent that they have read this Agreement and all of its Exhibits and attachments, they are aware of the contents, and that they agree to follow their terms.

_____	_____
Physician	Date of Signature
_____	_____
RN (Agent of the LPHA)	Date of Signature

Exhibit A: Medical Protocol

Mass Prophylaxis Treatment Clinics
Dispensing of Antibiotics

I direct Registered Professional Nurses (RNs) employed by, or serving as volunteers for, the _____ (name of agency), and working within the geographic area stated in the collaborative practice agreement, to dispense medications to individuals presenting for prophylactic treatment to a known or potentially harmful biological agent.

All medications must be dispensed in accordance with the following prophylactic treatment guidelines and within the restrictions of the guidelines of the Strategic National Stockpile program.

Recommended Post-exposure Prophylaxis for Inhalational Anthrax

Table 4. Recommended Therapy for Inhalational Anthrax Infection for Post-exposure Prophylaxis (PEP)

Category	Initial Oral Therapy+	Therapy if Strain is Susceptible#	Total Duration of PEP Therapy
Adults	Ciprofloxacin, 500 mg orally every 12h **Or** Doxycycline, 100 mg orally every 12h		60 days
Children	Ciprofloxacin Weight < 33 kg (73 lbs): 15 mg/kg orally every 12 h Weight ≥ 33 kg (73 lbs): adult dose **Or** Doxycycline Weight < 45 kg (99 lbs): 2.2 mg/kg orally every 12 hours Weight ≥ 45 kg (99 lbs): adult dose	Amoxicillin Weight < 20 kg (44 lbs): 80 mg/kg to be taken orally in 3 divided doses every 8 hr Weight ≥20 kg (44 lbs): 500 mg orally every 8 hr	60 days
Pregnant Women	Ciprofloxacin, 500 mg orally every 12 h **Or** Doxycycline, 100 mg orally every 12h	Amoxicillin, 500 mg orally every 8 h	60 days
Immunosuppressed persons	Same as for nonimmunosuppressed adults and children		

+ The Centers for Disease Control and Prevention (CDC) has stated that when no information is available about the antimicrobial susceptibility of the implicated strain of *Bacillus anthracis*, initial PEP with ciprofloxacin or doxycycline is recommended for adults and children. The Food and Drug Administration (FDA) has approved ciprofloxacin and doxycycline for use as PEP against anthrax.

CDC recommends that as soon as the organism's susceptibility to penicillin has been confirmed, prophylactic therapy for children and pregnant women should be changed to oral amoxicillin. Amoxicillin is not FDA-approved for anthrax PEP.

Modified from a table contained in Inglesby TV, O'Toole T, Henderson DA, et al. Anthrax as a biological weapon, 2002: updated recommendations for management. *JAMA* 2002; 287:2236-52. Includes corrections from *JAMA* 2002; 288:1849, and more recent information contained in CDC. Responding to detection of aerosolized Bacillus anthracis by autonomous detection systems in the workplace. *MMWR* 2004;53(No. RR-7):9, and in Marano N. Anthrax, CDC clinician Outreach and Communication Activity clinican Briefing, March 16, 2004.

Recommended Post-exposure Prophylaxis for Pneumonic Plague

Table 2. Working Group Recommendations for Treatment of Patients With Pneumonic Plague in the Contained and Mass Casualty Settings and for Postexposure Prophylaxis*

Patient Category	Recommended Therapy
	Mass Casualty Setting and Postexposure Prophylaxis#
Adults	Preferred choices Doxycycline, 100 mg orally twice daily†† Ciprofloxacin, 500 mg orally twice daily‡ Alternative choice Chloramphenicol, 25 mg/kg orally 4 times daily§**
Children‖	Preferred choice Doxycycline,†† If ≥45 kg, give adult dosage If <45 kg, then give 2.2 mg/kg orally twice daily Ciprofloxacin, 20 mg/kg orally twice daily Alternative choices Chloramphenicol, 25 mg/kg orally 4 times daily§**
Pregnant women¶	Preferred choices Doxycycline, 100 mg orally twice daily†† Ciprofloxacin, 500 mg orally twice daily Alternative choices Chloramphenicol, 25 mg/kg orally 4 times daily§**

*These are consensus recommendations of the Working Group on Civilian Biodefense and are not necessarily approved by the Food and Drug Administration. See "Therapy" section for explanations. One antimicrobial agent should be selected. Therapy should be continued for 10 days. Oral therapy should be substituted when patient's condition improves. IM indicates intramuscularly; IV, intravenously.

‡Other fluoroquinolones can be substituted at doses appropriate for age. Ciprofloxacin dosage should not exceed 1 g/d in children.

§Concentration should be maintained between 5 and 20 µg/mL. Concentrations greater than 25 µg/mL can cause reversible bone marrow suppression.[35,62]

‖Refer to "Management of Special Groups" for details. In children, ciprofloxacin dose should not exceed 1 g/d, chloramphenicol should not exceed 4 g/d. Children younger than 2 years should not receive chloramphenicol.

¶Refer to "Management of Special Groups" for details and for discussion of breastfeeding women. In neonates, gentamicin loading dose of 4 mg/kg should be given initially.[63]

#Duration of treatment of plague in mass casualty setting is 10 days. Duration of postexposure prophylaxis to prevent plague infection is 7 days.

**Children younger than 2 years should not receive chloramphenicol. Oral formulation available only outside the United States.

††Tetracycline could be substituted for doxycycline.

Inglesby TV, Dennis DT, Henderson DA, et al. Plague as a Biological Weapon: Medical and Public Health Management. JAMA 2000; 283:2281

Recommended Post-exposure Prophylaxis for Tularemia

Table 3. Working Group Consensus Recommendations for Treatment of Patients With Tularemia in a Mass Casualty Setting and for Postexposure Prophylaxis*

Mass Casualty Recommended Therapy
Adults
Preferred choices
Doxycycline, 100 mg orally twice daily
Ciprofloxacin, 500 mg orally twice daily†
Children
Preferred choices
Doxycycline; if ≥45 kg, give 100 mg orally twice daily; if <45 kg, give 2.2 mg/kg orally twice daily
Ciprofloxacin, 15 mg/kg orally twice daily†‡
Pregnant Women
Preferred choices
Ciprofloxacin, 500 mg orally twice daily†
Doxycycline, 100 mg orally twice daily

*One antibiotic, appropriate for patient age, should be chosen from among alternatives. The duration of all recommended therapies in Table 3 is 14 days.
†Not a US Food and Drug Administration–approved use.
‡Ciprofloxacin dosage should not exceed 1 g/d in children.

Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a Biological Weapon: Medical and Public Health Management. JAMA 2001; 285:2763-73-90.

One of the attached post-exposure prophylaxis dispensing algorithms must be followed (depending on the bacterial agent for which prophylaxis is being provided [i.e., *Bacillus anthracis, Yersinia pestis,* or *Francisella tularensis*] and on which drug is designated by the Missouri Department of Health and Senior Services as the primary prophylactic drug):

Attachment 1: Anthrax Post-Exposure Prophylaxis Dispensing Algorithm
Attachment 2: Tularemia Post-Exposure Prophylaxis Dispensing Algorithm
Attachment 3: Plague Post-Exposure Prophylaxis Dispensing Algorithm

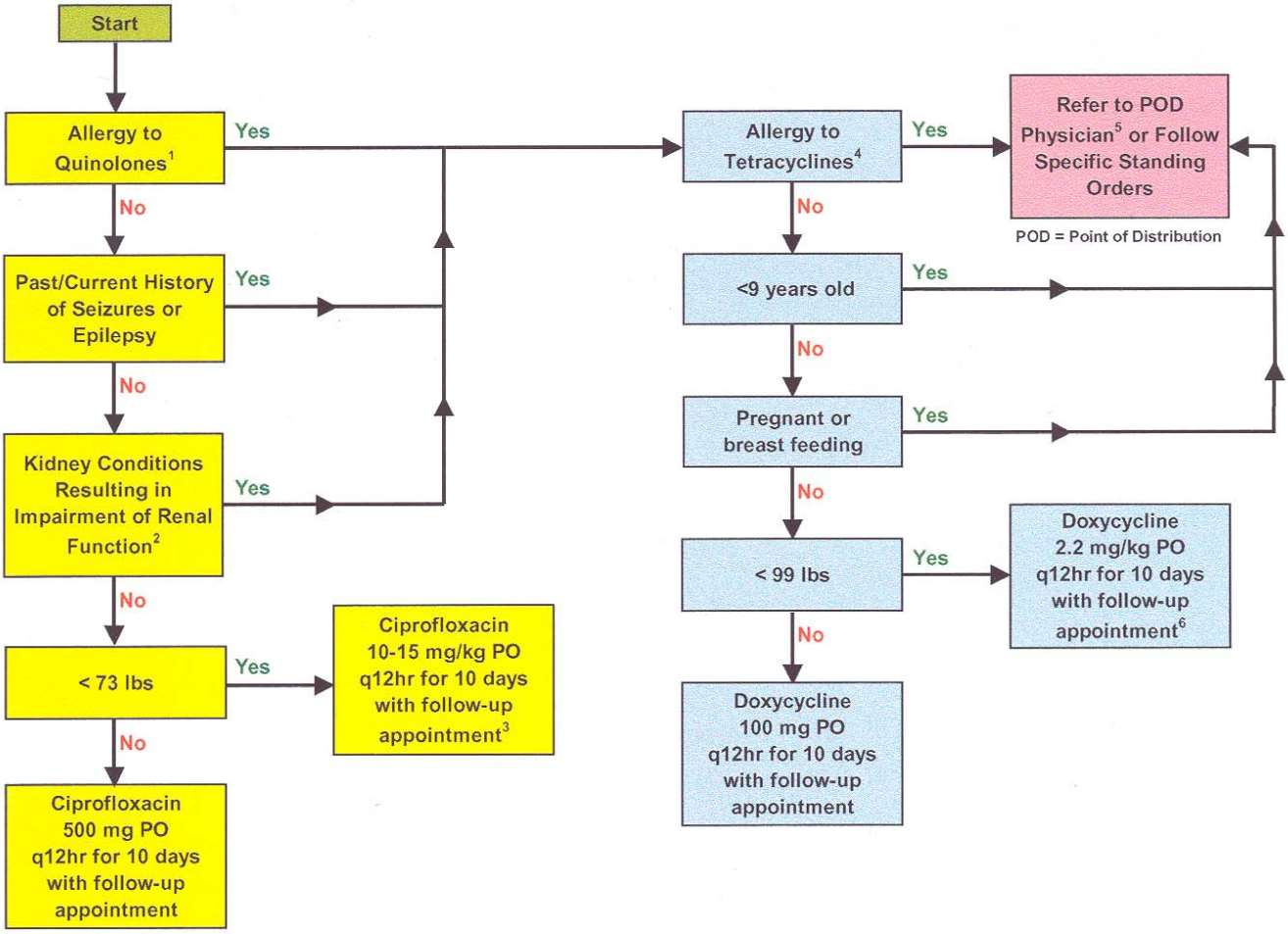
Review of this order, and agency policies and procedures related to carrying out this order, shall occur at least once every year.

This order will terminate on _____

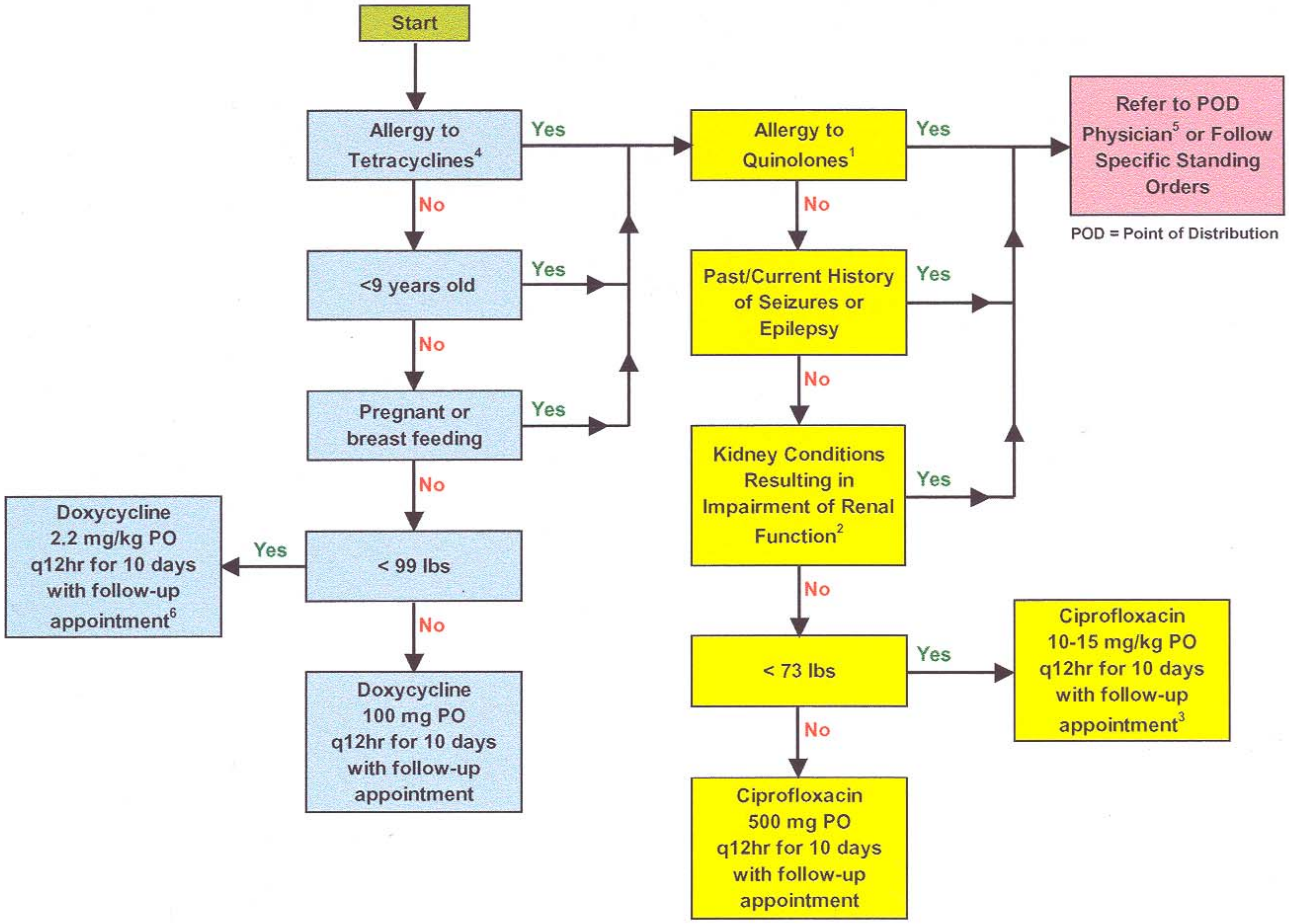
_____ _____
Physician Date of Signature

_____ _____
RN (Agent of the LPHA) Date of Signature

Anthrax Post-Exposure Prophylaxis Dispensing Algorithm
Primary Drug: Ciprofloxacin



Anthrax Post-Exposure Prophylaxis Dispensing Algorithm
Primary Drug: Doxycycline



Anthrax Post-Exposure Prophylaxis Dispensing Algorithm

The above flow diagrams and the footnotes on the next page describe antimicrobial drug selection and dosing information for persons requiring post-exposure prophylaxis (PEP) to prevent inhalational anthrax following potential exposure to aerosolized *Bacillus anthracis* spores.

Reports have been published of engineered strains of tetracycline-resistant and quinolone-resistant *B. anthracis*.[1,2] There is also a possibility for resistance to penicillins through induction of beta-lactamase enzymes. For these reasons, public health officials will test the antibiotic susceptibility of the implicated *B. anthracis* strain to determine drug selection. The most widely available, efficacious, and least toxic antibiotic will be dispensed for post-exposure prophylaxis based upon these susceptibility results,[1] and upon drug availability.

When no information is available about the antimicrobial susceptibility of the implicated strain of *B. anthracis*, initial PEP with ciprofloxacin or doxycycline is recommended for adults and children.[3,4] (See Appendix A for further comments on the use of these drugs for PEP in children and pregnant women, and in immunosuppressed persons. It has been recommended that as soon as the organism's susceptibility to penicillin has been confirmed, prophylactic therapy for children and pregnant women should be changed to oral amoxicillin.[3])

> Both ciprofloxacin and doxycycline are FDA-approved for inhalational anthrax PEP for both adults and children.[5,6]
>
> Amoxicillin has not been approved by FDA as therapy for inhalational anthrax PEP, although it is often recommended for this indication.[5] In an emergency situation in which Strategic National Stockpile (SNS)-supplied amoxicillin is used, the drug could be given under an investigational new drug (IND) protocol (with CDC staff being the principal investigators), or under an Emergency Use Authorization (EUA) mandate if a State of National Emergency is declared. If an EUA mandate is in place, an IND form does not need to be completed by recipients of the drug.
>
> *B. anthracis* is not susceptible to cephalosporins and trimethoprim-sulfamethoxazole; therefore, these agents should not be used for prophylaxis.[3]

Following a terrorist attack, the Missouri Department of Health and Senior Services (DHSS), in consultation with the Centers for Disease Control and Prevention (CDC), will designate which drug (i.e., ciprofloxacin or doxycycline) will be the primary drug to use for prophylaxis. It is very important that prophylactic antibiotics be started as soon as possible after actual or suspected inhalation of *B. anthracis* spores.

Ciprofloxacin (and other fluoroquinolones), penicillin, and doxycycline (and other tetracyclines) are each excreted in breast milk. Therefore, a breastfeeding woman should be treated or given prophylaxis with the same antibiotic as her infant based on what is most safe and effective for the infant.[1]

A total of 60 days of selected oral antibiotics (i.e., ciprofloxacin, doxycycline, or amoxicillin) should be dispensed to all persons potentially exposed to aerosolized *B. anthracis* spores. (In addition, CDC recommends, in conjunction with antibiotic prophylaxis, the use of a 3-dose regimen [0, 2 weeks, 4 weeks] of anthrax vaccine.[3] Use of the vaccine as part of PEP is not discussed further in this document.)

All persons for whom *B. anthracis* PEP is recommended should initially receive a 10-day supply of the appropriate antibiotic, along with a follow-up appointment to receive additional medication. The initial course of 10 days is recommended based upon the normal twice-a-day regimen of ciprofloxacin and doxycycline, and the availability of 20 tablets in unit-of-use containers from the SNS Program. At the follow-up visit, susceptibility data on the organism will be available and the medication may be changed.

All persons receiving PEP should be instructed to report immediately flu like symptoms or febrile illness to their physicians who should then evaluate the need to initiate immediate treatment for possible inhalational anthrax.

> Given the rapid course of symptomatic inhalational anthrax, early antibiotic administration is essential if this disease is suspected. A delay in initiating antibiotic treatment in patients with early signs/symptoms of inhalational anthrax may substantially lessen

chances for survival. Given the difficulty in achieving rapid microbiologic diagnosis of anthrax, all persons in high-risk groups who develop fever or evidence of systemic disease should start receiving therapy for possible anthrax as soon as possible while awaiting the results of laboratory studies.

The following numbered paragraphs provide additional comments on some of the individual steps contained in the two flow diagrams entitled "Anthrax Post-Exposure Prophylaxis Dispensing Algorithm – Primary Drug: Ciprofloxacin" and "Anthrax Post-Exposure Prophylaxis Dispensing Algorithm – Primary Drug: Doxycycline."

1. Quinolone drugs include: acrosoxacin or rosoxacin (Eradacil); cinoxacin (Cinobac); ciprofloxacin (Cipro, Ciloxan); gatafloxacin (Tequin); grepafloxacin (Raxar); levafloxacin (Levaquin, Quixin); lomefloxacin (Maxaquin); moxifloxacin (Avelox, ABC Pak); nadifloxacin (Acuatim); norfloxacin (Chibroxin, Noroxin); nalidixic acid (NegGram); ofloxacin (Floxin, Ocuflox); oxolinic acid; pefloxacin (Peflacine); rufloxacin; sparfloxacin (Zagam, Respipac); temafloxacin; trovafloxacin or alatrofloxacin (Trovan).

2. Included here are those who: 1) are receiving dialysis, 2) have known kidney failure (end-stage renal disease), or 3) have reduced kidney function for any reason. Patients who have chronic kidney infections or kidney stones can be given the full dose of antibiotic, unless they have been told by a medical professional that they have kidney damage.

3. For patients weighing less than 73 pounds (33 kilograms), the dosage of ciprofloxacin is 10-15 mg/kg[7] (as described in the chart below) by mouth every 12 hours.

Weight (pounds)	Weight (kilogram)	Dose (mg)	Available Dosage Forms of Ciprofloxacin				
			100mg tablet	250mg tablet	500mg tablet*	250mg/5mL suspension*	500mg/5mL suspension
7-12 lbs	3-5 kg	50 mg PO BID	½	¼		1 mL (1 bottle)	0.5 mL (1 bottle)
13-22 lbs	6-10 kg	100 mg PO BID	1			2 mL (1 bottle)	1 mL (1 bottle)
18-28 lbs	8-13 kg	125 mg PO BID		½	¼	2.5 mL (1 bottle)	1.25 mL (1 bottle)
22-33 lbs	10-15 kg	150 mg PO BID	1½			3 mL (1 bottle)	1.5 mL (1 bottle)
29-44 lbs	13-20 kg	200 mg PO BID	2			4 mL (1 bottle)	2 mL (1 bottle)
36-56 lbs	16-25 kg	250 mg PO BID		1	½	5 mL (1 bottle)	2.5 mL (1 bottle)
55-83 lbs	25-37 kg	375 mg PO BID		1½	¾	7.5 mL (2 bottles)	3.75 mL (1 bottle)
≥73 lbs	≥ 33 kg	500 mg PO BID		2	1	10 mL (2 bottles)	5 mL (1 bottle)

* Dosage Forms available through the CDC National Pharmaceutical Stockpile Program.

4. Tetracycline drugs include: demeclocycline (Declomycin); doxycycline (Adoxa, Bio-Tab, Doryx, Doxy, Monodox, Periostat, Vibra-Tabs, Vibramycin); minocycline (Arestin, Dynacin, Minocin, Vectrin); oxytetracycline (Terak, Terra-Cortril, Terramycin, Urobiotic-250); tetracycline (Achromycin V, Sumycin, Topicycline, Helidac).

5. Refer to the POD physician (i.e., the physican at, or consulting with, the point of dispensing [POD] site), or follow standing orders if these orders address the specific situation.

   As necessary, the POD physician can provide further assessment and drug selection. If the person reportedly cannot take ciprofloxacin and/or doxycycline because of a past allergic reaction(s), the physician should first confirm that this is the case. If it is determined that the person cannot safely take either of the recommended drugs, then another antimicrobial drug should be selected. DHSS, in consultation with CDC, will provide information on additional drug options. If doxycycline is used in pregnant women, periodic liver function testing should be performed.[1]

6. For patients weighing less than 99 pounds (45 kilograms), the dosage of doxycycline is 2.2 mg/kg (as described in the chart below) by mouth every 12 hours.

Weight (lbs)	Weight (kg)	Dose (mg)	Available Dosage Forms of Doxycycline				
			20mg tablet	50mg tablet or capsule	100mg tablet* or capsule	25mg/5mL suspension*	50mg/5mL syrup
5-10	2-5	10 mg PO BID				2 mL	1 mL
11-20	6-9	20 mg PO BID	1			4 mL	2 mL
21-30	10-14	30 mg PO BID				6 mL	3 mL
31-40	15-19	40 mg PO BID	2			8 mL	4 mL
41-50	20-22	50 mg PO BID		1	½ tablet	10 mL	5 mL
51-60	23-27	60 mg PO BID	3			12 mL	6 mL
61-70	28-32	70 mg PO BID				14 mL	7 mL
71-80	33-36	80 mg PO BID	4			16 mL	8 mL
81-90	37-41	90 mg PO BID				18 mL	9 mL
91-100	≥ 42	100 mg PO BID	5	2	1	20 mL	10 mL

*Dosage Forms available through the CDC National Pharmaceutical Stockpile Program

All persons who are provided with prophylactic medication will be given a written handout that includes, as appropriate, instructions on the following issues:

- **Persons already taking an antibiotic of the same drug class as that prescribed for prophylaxis.**

  If a person who is given a prophylactic antibiotic is already taking an antibiotic of the same drug class, he/she should stop the antibiotic he/she has been taking, begin taking the prophylactic antibiotic, and contact his/her medical provider for further instructions.

- **Interaction of ciprofloxacin with xanthine derivatives and probenecid.**

  The hepatic metabolism of the xanthine derivatives theophylline (Theo-Dur, Slo-BID, Slo-Phyllin, Uniphyl), aminophylline, and oxtriphylline (Choledyl SA) may be inhibited by ciprofloxacin, resulting in toxicity. If a person taking one of these drugs is given ciprofloxacin for prophylaxis, the dose of the xanthine derivative should be decreased by 50%. The individual should contact his/her medical provider for drug monitoring and possible further dosage adjustment.

  Probenecid (Benemid) may decrease the renal excretion of ciprofloxacin, therefore increasing the risk of ciprofloxacin toxicity. Consequently, if a person taking probenecid is given ciprofloxacin for prophylaxis, he/she should temporarily stop taking the probenecid. He/she should contact his/her medical provider regarding when to restart probenecid and whether a dosage adjustment is necessary.

- **Interaction of ciprofloxacin and doxycycline with warfarin.**

  Either ciprofloxacin or doxycycline may enhance the anticoagulant effects of warfarin (Coumadin). An individual who is given either ciprofloxacin or doxycycline for prophylaxis should contact his/her medical provider for monitoring and possible adjustment of warfarin dosage.

- **Interaction of doxycycline with oral contraceptives.**

  Oral contraceptives containing estrogen may be less effective if taken concurrently with doxycycline. Unplanned pregnancies may occur. A different or additional means of birth control should be utilized while taking doxycycline.

- **Other potential drug interactions.**

  The written handout will contain information on additional potential drug interactions.

References:

1. Inglesby TV, Henderson DA, Bartlett JG, et al. Anthrax as a biological weapon, 2002. *JAMA*. 2002;287:2236-2252.
   http://jama.ama-assn.org/cgi/content/full/287/17/2236

   See also "Guidelines for Treatment of Anthrax" in the **Letters** section of *JAMA* 2002;288:1848-9. Contained here are comments on the Inglesby, et al article, with a response from the authors. Also, immediately following the **Letters** section on page 1849 is a section entitled **Correction**, which lists changes to the treatment guidelines that were presented in the Inglesby article.
   http://jama.ama-assn.org/cgi/reprint/288/15/1848.pdf

2. Brook I, Elliott TB, Pryor HI, et al. In vitro resistance of *Bacillus anthracis* Sterne to doxycyline, macrolides and quinolones. *International Journal of Antimicrobial Agents*. 18(2001);559-562.

3. CDC. Responding to detection of aerosolized *Bacillus anthracis* by autonomous detection systems in the workplace. *MMWR* 2004; 53(RR07):8-9.
   http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5307a1.htm

4. Markenson D, Redlener I. Pediatric terrorism preparedness national guidelines and recommendations: findings of an evidenced-based consensus process. *Biosecur Bioterror* 2004; 2:301-19.

   This article contains pediatric recommendations and guidelines from a "cadre of experts and stakeholders from government agencies, professional organizations, emergency medicine and response, pediatrics, mental health, and disaster preparedness. . . . . These recommendations and guidelines represent the first national evidence-based standards for pediatric disaster and terrorism preparedness."

5. Letters: Guidelines for treatment of anthrax, and Correction. *JAMA* 2002; 288:1848-9.
   http://jama.ama-assn.org/cgi/content/full/288/15/1848

6. *Federal Register*: November 2, 2001 (Volume 66, Number 213):55679-82.
   http://www.fda.gov/OHRMS/DOCKETS/98fr/110201b.htm

7. CDC. Update: investigation of anthrax associated with intentional exposure and interim public health guidelines, October 2001. *MMWR* 2001; 50(41):89-893.
   http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5041a1.htm

Appendix A

Comments On the Use of Ciprofloxacin and Doxycycline for Anthrax Post-Exposure Prophylaxis in Children, Pregnant Women, and Immunosuppressed Persons

Working Group on Civilian Biodefense

(Inglesby TV, Henderson DA, Bartlett JG, et al. Anthrax as a biological weapon, 2002. *JAMA*. 2002;287:2248. http://jama.ama-assn.org/cgi/content/full/287/17/2236)

Children

It has been recommended that ciprofloxacin and other fluoroquinolones should not be used in children younger than 16 to 18 years because of a link to permanent arthropathy in adolescent animals and transient arthropathy in a small number of children. However, balancing these risks against the risks of anthrax infections caused by an engineered antibiotic-resistant strain, the working group recommends that ciprofloxacin be used as a component of combination therapy for children with inhalational anthrax. For post-exposure prophylaxis or following a mass casualty attack, the working group recommends monotherapy with fluoroquinolones.

The American Academy of Pediatrics [AAP] has recommended that doxycycline not be used in children younger than 9 years because the drug has resulted in retarded skeletal growth in infants and discolored teeth in infants and children [see below for further AAP comment]. However, the serious risk of infection following an anthrax attack supports the consensus recommendation that doxycycline, instead of ciprofloxacin, be used in children if antibiotic susceptibility testing, exhaustion of drug supplies, or adverse reactions preclude use of ciprofloxacin.

Pregnant Women

Fluoroquinolones are not generally recommended during pregnancy because of their known association with arthropathy in adolescent animals and small numbers of children. Animal studies have discovered no evidence of teratogenicity related to ciprofloxacin, but no controlled studies of ciprofloxacin in pregnant women have been conducted. Balancing these possible risks against the concerns of anthrax due to engineered antibiotic-resistant strains, the working group recommends that pregnant women receive ciprofloxacin as part of combination therapy for treatment of inhalational anthrax. We also recommend that pregnant women receive fluoroquinolones in the usual adult dosages for post-exposure prophylaxis or monotherapy treatment in the mass casualty setting.

The tetracycline class of antibiotics has been associated with both toxic effects in the liver in pregnant women and fetal toxic effects, including retarded skeletal growth. Balancing the risks of anthrax infection with those associated with doxycycline use in pregnancy, the working group recommends that doxycycline can be used as an alternative to ciprofloxacin as part of combination therapy in pregnant women for treatment of inhalational anthrax. For post-exposure prophylaxis or in mass casualty settings, doxycycline can also be used as an alternate to ciprofloxacin in pregnant women. If doxycycline is used in pregnant women, periodic liver function testing should be performed.

Ciprofloxacin (and other fluoroquinolones), penicillin, and doxycycline (and other tetracyclines) are each excreted in breast milk. Therefore, a breastfeeding woman should be treated or given prophylaxis with the same antibiotic as her infant based on what is most safe and effective for the infant.

Immunosuppressed Persons

Post-exposure prophylaxis for anthrax among those who are immunosuppressed has not been studied in human or animal models of anthrax infection. Therefore, the working group consensus recommends administering antibiotics in the same regimens recommended for immunocompetent adults and children.

American Academy of Pediatrics

American Academy of Pediatrics. Anthrax. In: Pickering LK, ed. *Red Book: 2003 Report of the Committee on Infectious Diseases*. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2003:199.

On the basis of limited available data, the best means for prevention of inhalation anthrax after exposure to *B anthracis* spores is prolonged antimicrobial therapy in conjunction with a 3-dose regimen (at 0, 2, and 4 weeks) of anthrax immunization.

When no information is available about the antimicrobial susceptibility of the implicated strain of *B anthracis*, initial post-exposure prophylaxis for adults or children with ciprofloxacin or doxycycline is recommended. Although fluoroquinolones and tetracyclines are not recommended as first-choice drugs in children because of adverse effects, these concerns may be outweighed by the need for early treatment of pregnant women and children exposed to *B anthracis* after a terrorist attack. As soon as susceptibility of the organism to penicillin has been confirmed, prophylactic therapy for children should be changed to oral amoxicillin, 80 mg/kg per day, divided every 8 hours (not to exceed 500mg, 3 times/day).

American College of Obstetricians and Gynecologists

American College of Obstetricians and Gynecologists. Hale RW, Zinberg S. Dear Colleague Letter. November 8, 2001. http://www.acog.org/from_home/misc/anthrax.cfm

Management of Exposed Asymptomatic Pregnant or Lactating Women

At this time the Committee on Obstetric Practice recommends that prophylaxis of asymptomatic pregnant and lactating women be limited to those women who have had exposure to a confirmed environmental contamination or who are exposed to a high risk source as determined by the local Department of Health. Prophylaxis for asymptomatic pregnant or lactating women is as follows:

- ciprofloxacin 500 mg p.o. every 12 hours x 60 days.

Ciprofloxacin and other fluoroquinolones are generally not used during pregnancy and lactation because of studies suggesting irreversible drug-induced arthropathy in a variety of species of adolescent animals. However, no clear evidence of teratogenicity has been demonstrated in humans. Despite these concerns, the potential morbidity and mortality from anthrax clearly outweighs these risks. Thus, if the bacteria are shown to be sensitive to penicillin, the treatment should be switched to amoxicillin 500 mg p.o. TID x 60 days.

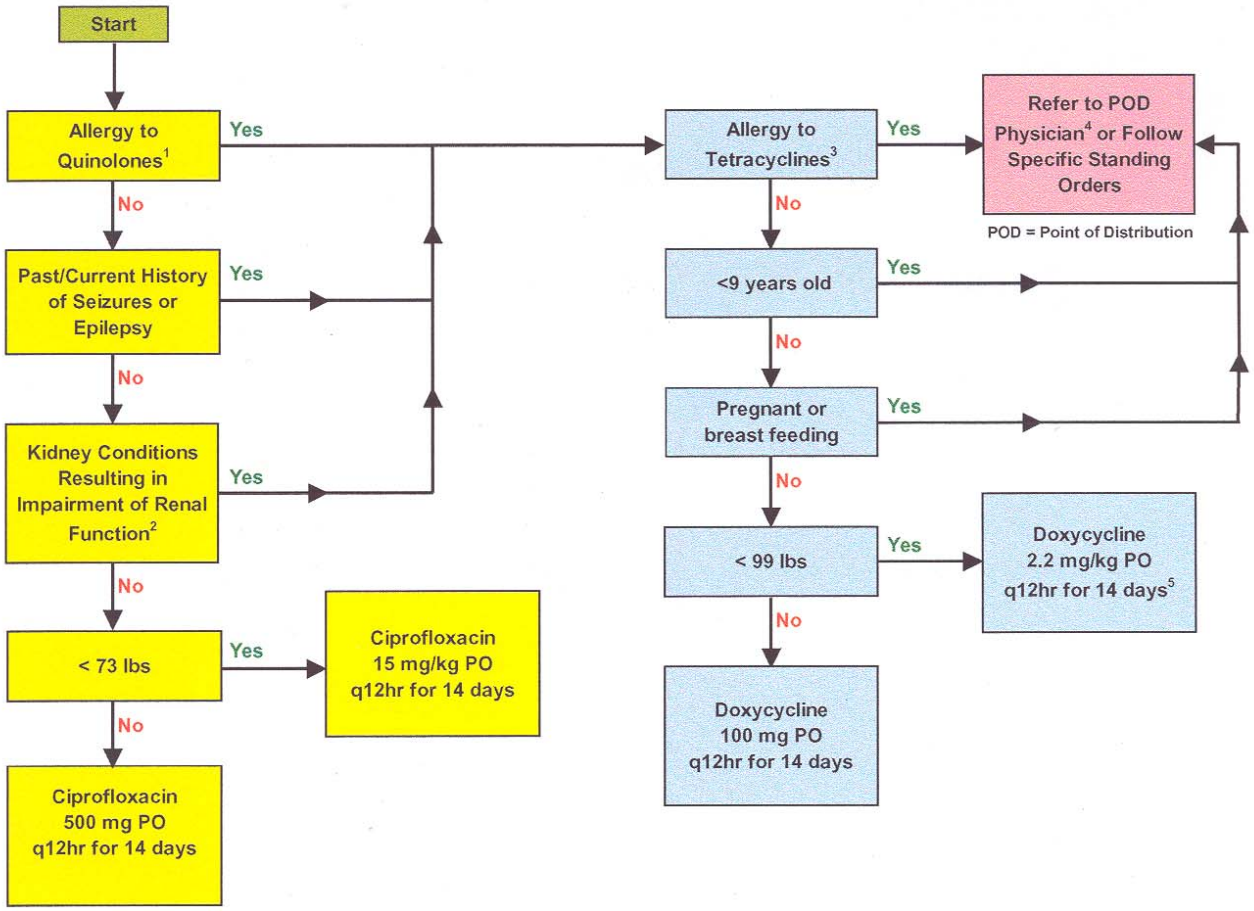
If a woman has been prescribed ciprofloxacin and is found to be pregnant, she should continue her course of antibiotics for the full 60 days unless the bacteria is shown to be penicillin-sensitive she should then be switched to amoxicillin. A 1999 expert review of published data on experiences with ciprofloxacin concluded that therapeutic doses during pregnancy are unlikely to pose substantial teratogenic risk but the data are insufficient to state that there is no risk. In the case of penicillin and ciprofloxacin-allergic patients, treatment should consist of doxycycline or consider penicillin desensitization if the organism is proven sensitive. In this situation, the risks of anthrax would far out weigh the risks of doxycycline to the fetus (i.e., dental staining of the primary teeth and possible depressed bone growth and defective dental enamel).

Markenson D, Redlener I. Pediatric terrorism preparedness national guidelines and recommendations: findings of an evidenced-based consensus process. *Biosecur Bioterror* 2004; 2:301-19.

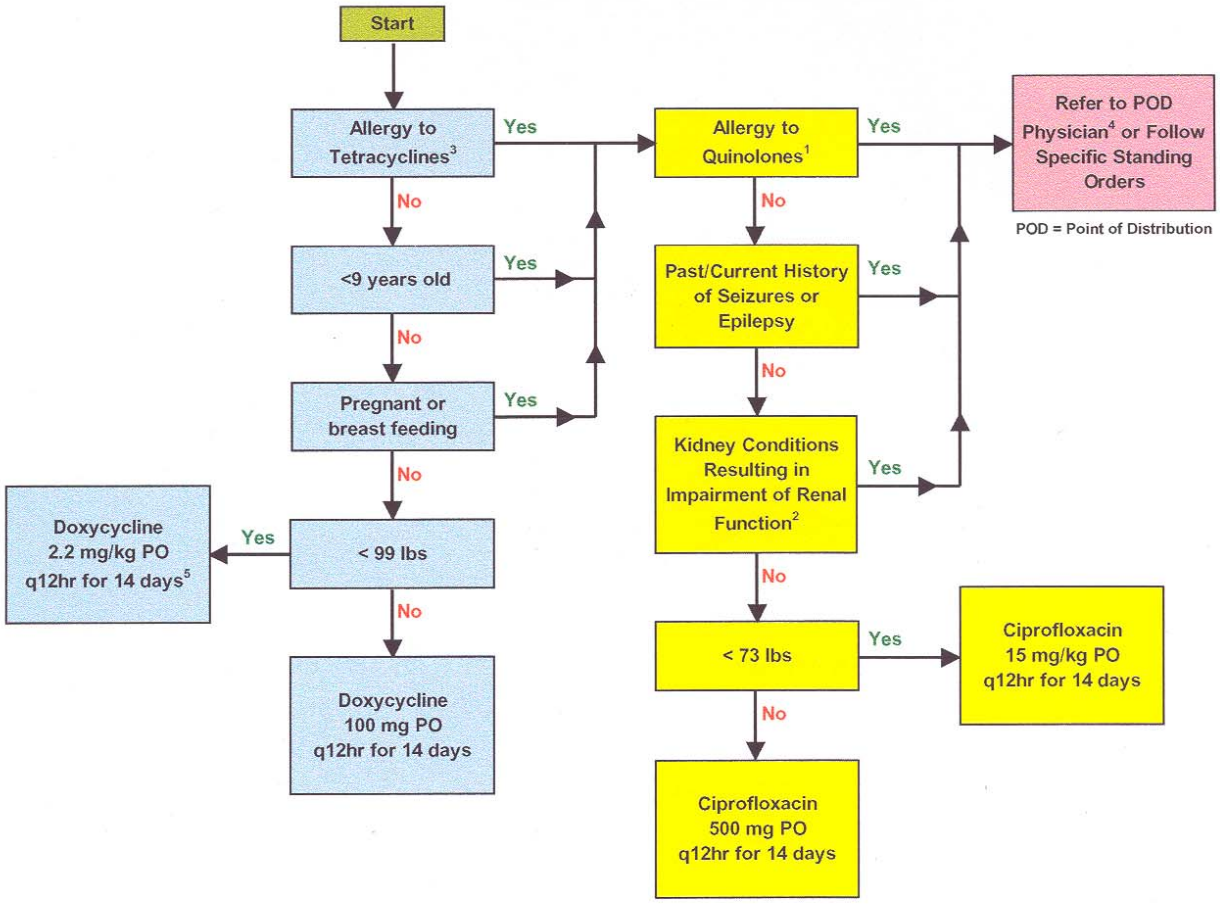
Ciprofloxacin or doxycycline (60-day course) is recommended for post-exposure prophylaxis for inhalational anthrax in children.

Children may be switched to oral amoxicillin (40–80 mg/kg/d divided q8h) to complete a 60-day course (assuming the organism is sensitive). It is recommended that the first 14 days of therapy or post-exposure prophylaxis, however, include ciprofloxacin and/or doxycycline regardless of age.

Tularemia Post-Exposure Prophylaxis Dispensing Algorithm
Primary Drug: Ciprofloxacin



Tularemia Post-Exposure Prophylaxis Dispensing Algorithm
Primary Drug: Doxycycline



Tularemia Post-Exposure Prophylaxis Dispensing Algorithm

The above flow diagrams and the footnotes on the next page describe antimicrobial drug selection and dosing information for persons requiring post-exposure prophylaxis (PEP) to prevent tularemia following potential exposure to aerosolized *Francisella tularensis*.

The Soviet Union's bioweapons program reportedly produced strains of *F. tularensis* engineered to be resistant to antibiotics. Transformed plasmids have been engineered to express tetracycline resistance in *F. tularensis*.[1] Since it is unknown whether a drug-resistant organism might be used in a bioterrorist event, public health officials will test the antibiotic susceptibility of the implicated *F. tularensis* strain to determine drug selection. The most widely available, efficacious, and least toxic antibiotic will be dispensed for post-exposure prophylaxis based upon these susceptibility results, and upon drug availability.

When no information is available about the antimicrobial susceptibility of the implicated strain of *B. anthracis*, initial PEP with oral doxycycline or ciprofloxacin is recommended for adults and children.[1]

> Doxycycline is FDA-approved for tularemia PEP.
>
> Ciprofloxacin has not been approved by FDA for tularemia PEP. In an emergency situation in which Strategic National Stockpile (SNS)-supplied ciprofloxacin is used, the drug could be given under an investigational new drug (IND) protocol (with CDC staff being the principal investigators), or under an Emergency Use Authorization (EUA) mandate if a State of National Emergency is declared. If an EUA mandate is in place, an IND form does not need to be completed by recipients of the drug.

Following a terrorist attack, the Missouri Department of Health and Senior Services (DHSS), in consultation with the Centers for Disease Control and Prevention (CDC), will designate which drug (i.e., doxycycline or ciprofloxacin) will be the primary drug to use for prophylaxis. It is very important that prophylactic antibiotics be started as soon as possible after actual or suspected inhalation of *F. tularensis*.

All persons for whom *F. tularensis* PEP is recommended should receive a 14-day supply of the appropriate antibiotic.

All persons receiving PEP should be instructed to report immediately flu likesymptoms or febrile illness to their physicians who should then evaluate the need to initiate immediate treatment for possible tularemia.

The following numbered paragraphs provide additional comments on some of the individual steps contained in the two flow diagrams entitled "Tularemia Post-Exposure Prophylaxis Dispensing Algorithm – Primary Drug: Doxycycline" and "Tularemia Post-Exposure Prophylaxis Dispensing Algorithm – Primary Drug: Ciprofloxacin."

1. Quinolone drugs include: acrosoxacin or rosoxacin (Eradacil); cinoxacin (Cinobac); ciprofloxacin (Cipro, Ciloxan); gatafloxacin (Tequin); grepafloxacin (Raxar); levafloxacin (Levaquin, Quixin); lomefloxacin (Maxaquin); moxifloxacin (Avelox, ABC Pak); nadifloxacin (Acuatim); norfloxacin (Chibroxin, Noroxin); nalidixic acid (NegGram); ofloxacin (Floxin, Ocuflox); oxolinic acid; pefloxacin (Peflacine); rufloxacin; sparfloxacin (Zagam, Respipac); temafloxacin; trovafloxacin or alatrofloxacin (Trovan).

2. Included here are those who: 1) are receiving dialysis, 2) have known kidney failure (end-stage renal disease), or 3) have reduced kidney function for any reason. Patients who have chronic kidney infections or kidney stones can be given the full dose of antibiotic, unless they have been told by a medical professional that they have kidney damage.

3. Tetracycline drugs include: demeclocycline (Declomycin); doxycycline (Adoxa, Bio-Tab, Doryx, Doxy, Monodox, Periostat, Vibra-Tabs, Vibramycin); minocycline (Arestin, Dynacin, Minocin, Vectrin); oxytetracycline (Terak, Terra-Cortril, Terramycin, Urobiotic-250); tetracycline (Achromycin V, Sumycin, Topicycline, Helidac).

4. Refer to the POD physician (i.e., the physican at, or consulting with, the point of dispensing [POD] site), or follow standing orders if these orders address the specific situation.

   As necessary, the POD physician can provide further assessment and drug selection. If the person reportedly cannot take ciprofloxacin and/or doxycycline because of a past allergic reaction(s), the physician should first confirm that this

is the case. If it is determined that the person cannot safely take either of the recommended drugs, then another antimicrobial drug should be selected. DHSS, in consultation with CDC, will provide information on additional drug options.

5. For patients weighing less than 99 pounds (45 kilograms), the dosage of doxycycline is 2.2 mg/kg (as described in the chart below) by mouth every 12 hours.

Weight (lbs)	Weight (kg)	Dose (mg)	Available Dosage Forms of Doxycycline				
			20mg tablet	50mg tablet or capsule	100mg tablet* or capsule	25mg/5mL suspension*	50mg/5mL syrup
5-10	2-5	10 mg PO BID				2 mL	1 mL
11-20	6-9	20 mg PO BID	1			4 mL	2 mL
21-30	10-14	30 mg PO BID				6 mL	3 mL
31-40	15-19	40 mg PO BID	2			8 mL	4 mL
41-50	20-22	50 mg PO BID		1	½ tablet	10 mL	5 mL
51-60	23-27	60 mg PO BID	3			12 mL	6 mL
61-70	28-32	70 mg PO BID				14 mL	7 mL
71-80	33-36	80 mg PO BID	4			16 mL	8 mL
81-90	37-41	90 mg PO BID				18 mL	9 mL
91-100	≥ 42	100 mg PO BID	5	2	1	20 mL	10 mL

*Dosage Forms available through the CDC National Pharmaceutical Stockpile Program

All persons who are provided with prophylactic medication will be given a written handout that includes, as appropriate, instructions on the following issues:

- **Persons already taking an antibiotic of the same drug class as that prescribed for prophylaxis.**

  If a person who is given a prophylactic antibiotic is already taking an antibiotic of the same drug class, he/she should stop the antibiotic he/she has been taking, begin taking the prophylactic antibiotic, and contact his/her medical provider for further instructions.

- **Interaction of ciprofloxacin with xanthine derivatives and probenecid.**

  The hepatic metabolism of the xanthine derivatives theophylline (Theo-Dur, Slo-BID, Slo-Phyllin, Uniphyl), aminophylline, and oxtriphylline (Choledyl SA) may be inhibited by ciprofloxacin, resulting in toxicity. If a person taking one of these drugs is given ciprofloxacin for prophylaxis, the dose of the xanthine derivative should be decreased by 50%. The individual should contact his/her medical provider for drug monitoring and possible further dosage adjustment.

  Probenecid (Benemid) may decrease the renal excretion of ciprofloxacin, therefore increasing the risk of ciprofloxacin toxicity. Consequently, if a person taking probenecid is given ciprofloxacin for prophylaxis, he/she should temporarily stop taking the probenecid. He/she should contact his/her medical provider regarding when to restart probenecid and whether a dosage adjustment is necessary.

- **Interaction of ciprofloxacin and doxycycline with warfarin.**

  Either ciprofloxacin or doxycycline may enhance the anticoagulant effects of warfarin (Coumadin). An individual who is given either ciprofloxacin or doxycycline for prophylaxis should contact his/her medical provider for monitoring and possible adjustment of warfarin dosage.

- **Interaction of doxycycline with oral contraceptives.**

  Oral contraceptives containing estrogen may be less effective if taken concurrently with doxycycline. Unplanned pregnancies may occur. A different or additional means of birth control should be utilized while taking doxycycline.

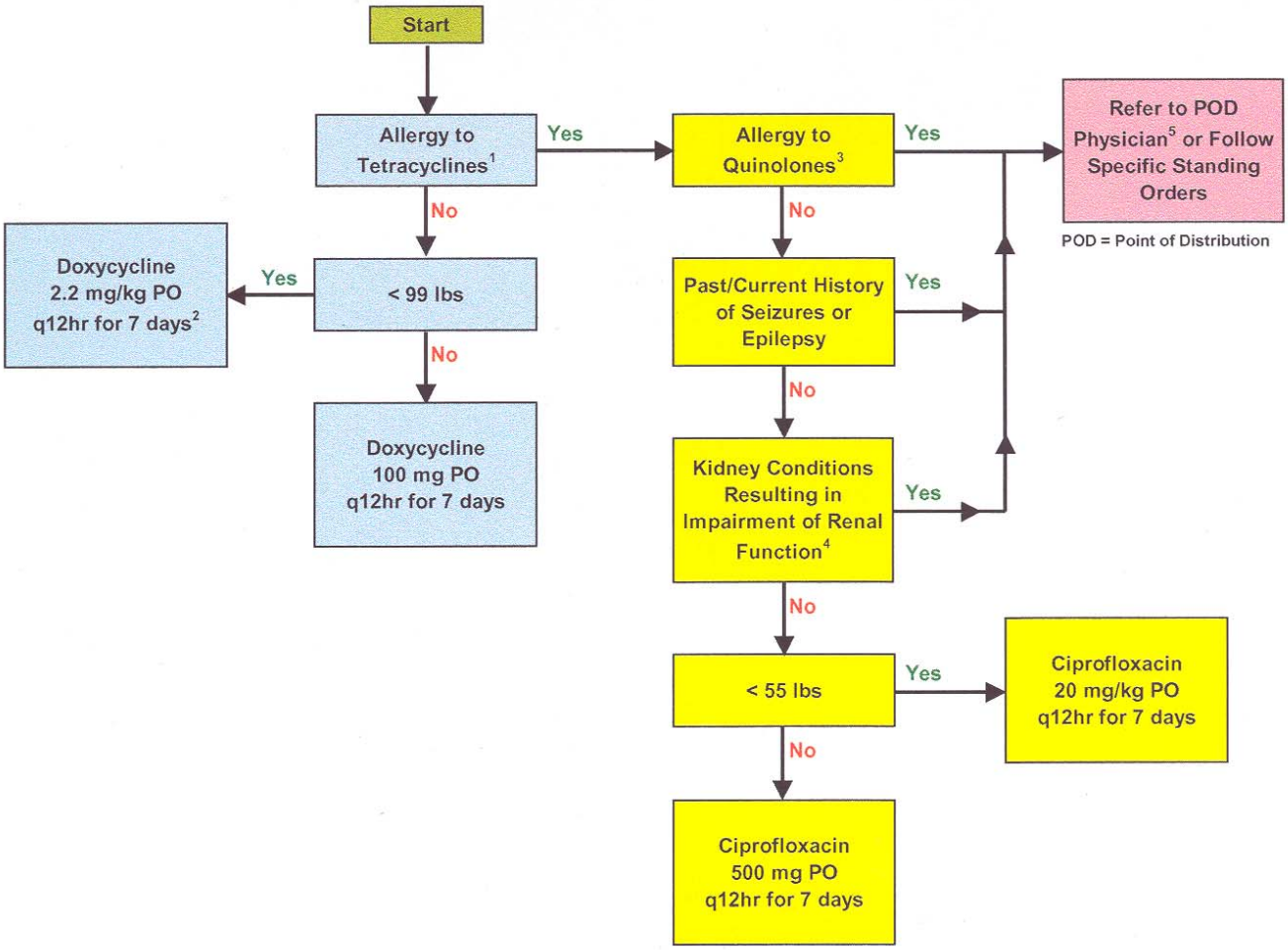
- **Other potential drug interactions.**

  The written handout will contain information on additional potential drug interactions.

References:

1. Dennis DT, et al. Tularemia as a Biological Weapon. *JAMA* 2001; 285(21):2763-73. http://jama.ama-assn.org/cgi/content/full/285/21/2763

Plague Post-Exposure Prophylaxis Dispensing Algorithm
Primary Drug: Doxycycline



Plague Post-Exposure Prophylaxis Dispensing Algorithm

The above flow diagram and the footnotes on the next page describe antimicrobial drug selection and dosing information for persons requiring post-exposure prophylaxis (PEP) to prevent plague following potential exposure to aerosolized *Yersinia pestis*. Included here would be:

a) asymptomatic persons who have potentially been recently exposed to aerosolized *Y. pestis* during a bioterrorist attack.
b) asymptomatic persons who have had recent household, hospital, or other close contact with persons with untreated pneumonic plague. (Close contact is defined as contact with a patient at less than 2 meters.)

Antibiotic resistance patterns of the implicated strain of *Y. pestis* must be considered in making treatment recommendations. Naturally occurring antibiotic resistance to the tetracycline class of drugs has occurred rarely with *Y. pestis*. Recently, a plasmid-mediated multidrug-resistant strain was isolated in Madagascar. A report published by Russian scientists cited quinolone-resistant *Y. pestis*. There have been assertions that Russian scientists have engineered multidrug-resistant strains of *Y. pestis*, although there is as yet no scientific publication confirming this.[1] Public health officials will test the antibiotic susceptibility of the implicated *Y. pestis* strain to determine drug selection. The most widely available, efficacious, and least toxic antibiotic will be dispensed for PEP based upon these susceptibility results, and upon drug availability.

When no information is available about the antimicrobial susceptibility of the implicated strain of *Y. pestis*, doxycycline is recommended as the first choice antibiotic for initial PEP for adults and children. Ciprofloxacin is also recommended as a preferred choice for PEP.[1,2]

(See Appendix A for further comments on the use of these drugs for PEP in children and pregnant women.)

Doxycycline is FDA-approved for plague PEP.[1]

Ciprofloxacin has not been approved by FDA for plague PEP, although it has been recommended for this indication.[1] In an emergency situation in which Strategic National Stockpile (SNS)-supplied ciprofloxacin is used, the drug could be given under an investigational new drug (IND) protocol (with CDC staff being the principal investigators), or under an Emergency Use Authorization (EUA) mandate if a State of National Emergency is declared. If an EUA mandate is in place, an IND form does not need to be completed by recipients of the drug.

It is very important that prophylactic antibiotics be started as soon as possible after actual or suspected exposure to *Y. pestis*.

Duration of PEP is 7 days.

The unit-of-use containers from the SNS Program contain a 10-day supply of medication, so the individual would be instructed to take a complete 7-day course of the antibiotic, and then discard the medication that remains in the container.

All persons receiving PEP should be instructed to report immediately febrile illness or new cough to their physicians who should then evaluate the need to initiate immediate treatment for possible plague.

The following numbered paragraphs provide additional comments on some of the individual steps contained in the flow diagram entitled "Plague Post-Exposure Prophylaxis Dispensing Algorithm – Primary Drug: Doxycycline."

1. Tetracycline drugs include: demeclocycline (Declomycin); doxycycline (Adoxa, Bio-Tab, Doryx, Doxy, Monodox, Periostat, Vibra-Tabs, Vibramycin); minocycline (Arestin, Dynacin, Minocin, Vectrin); oxytetracycline (Terak, Terra-Cortril, Terramycin, Urobiotic-250); tetracycline (Achromycin V, Sumycin, Topicycline, Helidac).

2. For patients weighing less than 99 pounds (45 kilograms), the dosage of doxycycline is 2.2 mg/kg (as described in the chart below) by mouth every 12 hours.

Weight (lbs)	Weight (kg)	Dose (mg)	Available Dosage Forms of Doxycycline				
			20mg tablet	50mg tablet or capsule	100mg tablet* or capsule	25mg/5mL suspension*	50mg/5mL syrup
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11-20	6-9	20 mg PO BID	1			4 mL	2 mL
21-30	10-14	30 mg PO BID				6 mL	3 mL
31-40	15-19	40 mg PO BID	2			8 mL	4 mL
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51-60	23-27	60 mg PO BID	3			12 mL	6 mL
61-70	28-32	70 mg PO BID				14 mL	7 mL
71-80	33-36	80 mg PO BID	4			16 mL	8 mL
81-90	37-41	90 mg PO BID				18 mL	9 mL
91-100	≥ 42	100 mg PO BID	5	2	1	20 mL	10 mL

*Dosage Forms available through the CDC National Pharmaceutical Stockpile Program

3. Quinolone drugs include: acrosoxacin or rosoxacin (Eradacil); cinoxacin (Cinobac); ciprofloxacin (Cipro, Ciloxan); gatafloxacin (Tequin); grepafloxacin (Raxar); levafloxacin (Levaquin, Quixin); lomefloxacin (Maxaquin); moxifloxacin (Avelox, ABC Pak); nadifloxacin (Acuatim); norfloxacin (Chibroxin, Noroxin); nalidixic acid (NegGram); ofloxacin (Floxin, Ocuflox); oxolinic acid; pefloxacin (Peflacine); rufloxacin; sparfloxacin (Zagam, Respipac); temafloxacin; trovafloxacin or alatrofloxacin (Trovan).

4. Included here are those who: 1) are receiving dialysis, 2) have known kidney failure (end-stage renal disease), or 3) have reduced kidney function for any reason. Patients who have chronic kidney infections or kidney stones can be given the full dose of antibiotic, unless they have been told by a medical professional that they have kidney damage.

5. Refer to the POD physician (i.e., the physican at, or consulting with, the point of dispensing [POD] site), or follow standing orders if these orders address the specific situation.

   As necessary, the POD physician can provide further assessment and drug selection. If the person reportedly cannot take doxycycline and/or ciprofloxacin because of a past allergic reaction(s), the physician should first confirm that this is the case. If it is determined that the person cannot safely take either of the recommended drugs, then another antimicrobial drug should be selected. The Missouri Department of Health and Senior Services (DHSS), in consultation with the Centers for Disease Control and Prevention (CDC), will provide information on additional drug options.

All persons who are provided with prophylactic medication will be given a written handout that includes, as appropriate, instructions on the following issues:

- **Persons already taking an antibiotic of the same drug class as that prescribed for prophylaxis.**

If a person who is given a prophylactic antibiotic is already taking an antibiotic of the same drug class, he/she should stop the antibiotic he/she has been taking, begin taking the prophylactic antibiotic, and contact his/her medical provider for further instructions.

- **Interaction of ciprofloxacin with xanthine derivatives and probenecid.**

  The hepatic metabolism of the xanthine derivatives theophylline (Theo-Dur, Slo-BID, Slo-Phyllin, Uniphyl), aminophylline, and oxtriphylline (Choledyl SA) may be inhibited by ciprofloxacin, resulting in toxicity. If a person taking one of these drugs is given ciprofloxacin for prophylaxis, the dose of the xanthine derivative should be decreased by 50%. The individual should contact his/her medical provider for drug monitoring and possible further dosage adjustment.

  Probenecid (Benemid) may decrease the renal excretion of ciprofloxacin, therefore increasing the risk of ciprofloxacin toxicity. Consequently, if a person taking probenecid is given ciprofloxacin for prophylaxis, he/she should temporarily stop taking the probenecid. He/she should contact his/her medical provider regarding when to restart probenecid and whether a dosage adjustment is necessary.

- **Interaction of ciprofloxacin and doxycycline with warfarin.**

  Either ciprofloxacin or doxycycline may enhance the anticoagulant effects of warfarin (Coumadin). An individual who is given either ciprofloxacin or doxycycline for prophylaxis should contact his/her medical provider for monitoring and possible adjustment of warfarin dosage.

- **Interaction of doxycycline with oral contraceptives.**

  Oral contraceptives containing estrogen may be less effective if taken concurrently with doxycycline. Unplanned pregnancies may occur. A different or additional means of birth control should be utilized while taking doxycycline.

- **Other potential drug interactions.**

  The written handout will contain information on additional potential drug interactions.

References:

1. Inglesby TV, et al. Plague as a biological weapon. *JAMA*, 2000; 283(17): 2281-90. http://jama.ama-assn.org/cgi/content/full/283/17/2281

2. Markenson D, Redlener I. Pediatric terrorism preparedness national guidelines and recommendations: findings of an evidenced-based consensus process. *Biosecur Bioterror* 2004; 2:301-19.

   This article contains pediatric recommendations and guidelines from a "cadre of experts and stakeholders from government agencies, professional organizations, emergency medicine and response, pediatrics, mental health, and disaster preparedness. . . . . These recommendations and guidelines represent the first national evidence-based standards for pediatric disaster and terrorism preparedness."

Appendix A

Comments on the Use of Ciprofloxacin and Doxycycline for Plague Post-Exposure Prophylaxis in Children, Pregnant Women, and Immunosuppressed Persons

Working Group on Civilian Biodefense

Inglesby TV, et al. Plague as a biological weapon. *JAMA*, 2000; 283(17): 2281-90. (http://jama.ama-assn.org/cgi/content/full/283/17/2281)

Consensus recommendations for special groups as set forth in the following reflect the clinical and evidence-based judgments of the working group and do not necessarily correspond to FDA approved use, indications, or labeling.

Children

Children aged 8 years and older can be treated with tetracycline antibiotics safely. However, in children younger than 8 years, tetracycline antibiotics may cause discolored teeth, and rare instances of retarded skeletal growth have been reported in infants. Some concern exists that fluoroquinolone use in children may cause arthropathy, although fluoroquinolones have been used to treat serious infections in children. No comparative studies assessing efficacy or safety of alternative treatment strategies for plague in children have or can be performed.

Given these considerations, for post-exposure prophylaxis the working group recommends that doxycycline be used. Alternatives include ciprofloxacin. The working group assessment is that the potential benefits of these antimicrobials in the treating of pneumonic plague infection substantially outweigh the risks.

Pregnant Women

The tetracycline class of antibiotics has been associated with fetal toxicity including retarded skeletal growth, although a large case-control study of doxycycline use in pregnancy showed no significant increase in teratogenic risk to the fetus. Liver toxicity has been reported in pregnant women following large doses of intravenous tetracycline (no longer sold in the United States), but it has also been reported following oral administration of tetracycline to nonpregnant individuals.

The working group recommends that pregnant women receive oral doxycycline for post-exposure prophylaxis. If the patient is unable to take doxycycline or the medication is unavailable, ciprofloxacin would be recommended.

The working group recommendation for treatment of breastfeeding women is to provide the mother and infant with the same antibiotic based on what is most safe and effective for the infant.

Immunosuppressed Persons

Post-exposure prophylaxis for pneumonic plague among those who are immunosuppressed has not been studied in human or animal models of pneumonic plague infection. Therefore, the consensus recommendation is to administer antibiotics according to the guidelines developed for immunocompetent adults and children.

American Academy of Pediatrics

American Academy of Pediatrics. Anthrax. In: Pickering LK, ed. *Red Book: 2003 Report of the Committee on Infectious Diseases*. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2003:489.

People with close exposure to a patient with pneumonic plague should receive antimicrobial prophylaxis. For adults and children 8 years of age and older and for children younger than 8 years of age at high risk, doxycycline is recommended. Prophylaxis is given for 7 days in the usual therapeutic doses.

Markenson D, Redlener I. Pediatric terrorism preparedness national guidelines and recommendations: findings of an evidenced-based consensus process. *Biosecur Bioterror* 2004; 2:301-19.

Doxycycline or ciprofloxacin are recommended for post-exposure prophylaxis for plague in children.

Anthrax

What is anthrax?
Anthrax is a serious disease caused by *Bacillus anthracis*, a bacteria that forms spores. A spore is a cell that is dormant (asleep) but may come to life under the right conditions. Spores can survive outside the body for long periods of time.

There are three types of anthrax, which involve the:

1. Skin (**cutaneous anthrax**) - The first symptom is a raised itchy bump that resembles an insect bite but within 1-2 days develops into a blister and then a painless ulcer with a characteristic black necrotic (dying) area in the center. Fever and painful swollen lymph nodes can be present.
2. Lungs (**inhalational anthrax**) - The first symptoms are flu-like and can include fever, fatigue, cough, muscle aches, nausea/vomiting, and sweating. Later symptoms include high fever, chest pain, severe breathing problems, and shock. (But don't assume that just because a person has cold or flu symptoms, he/she has inhalational anthrax.)
3. Digestive system (**gastrointestinal anthrax**) - The first symptoms are nausea, loss of appetite, bloody diarrhea, and fever, followed by bad stomach pain.

How do you get it?
Humans can become infected with anthrax by handling products from infected animals or by breathing in anthrax spores from infected animal products (like wool, for example). People can become infected with gastrointestinal anthrax by eating undercooked meat from infected animals.

Anthrax spores could be used by terrorists to intentionally cause illness and death. In 2001, anthrax was deliberately spread through the U.S. postal system by sending letters with powder containing anthrax spores. This caused 22 cases of anthrax, including 5 deaths.

Persons with inhalational anthrax cannot spread infection to others. With cutaneous anthrax, spread to others is very rare.

How soon do infected people get sick?
Symptoms can appear within 7 days of coming in contact with anthrax spores for all three types of the disease. For inhalation anthrax, symptoms can appear within a week or can take up to 42 days (and possibly longer) to appear.

How dangerous is anthrax? Is there a treatment?
Antibiotics are used to treat all three types of anthrax. Treatment is usually for 60 days. Success depends on the type of anthrax and how soon treatment begins.

Usually early treatment with antibiotics will cure cutaneous anthrax. Even if untreated, 80% of people with cutaneous anthrax do not die. Gastrointestinal anthrax is more serious, resulting in death in 25-60% of cases. Inhalational anthrax is much more severe. In the 2001 outbreak, about half of the cases of inhalational anthrax ended in death; in previous outbreaks, the death rate has been much higher. Early identification and treatment are important.

Can a person who is exposed to anthrax spores be treated so that they will not become sick?
If a person is thought to have recently breathed in anthrax spores, they will be given an antibiotic (such as ciprofloxacin or doxycycline) for 60 days, and may additionally be given 3 doses of anthrax vaccine, to prevent illness from occurring.

Is there a vaccine for anthrax?
There is a vaccine for anthrax that may be given as described in the answer to the preceding question following exposure to anthrax spores. Routine anthrax vaccination of the general public is not recommended.

What should I do if I think I have anthrax?
If you are showing symptoms of anthrax infection, call your health-care provider right away.

What should I do if I think I have been exposed to anthrax?
Contact local law enforcement officials immediately if you think that you may have been exposed to anthrax. This includes being exposed to a suspicious package or envelope that contains powder.

What should I do if cases of anthrax start to occur in my community?

Your local health department and the Missouri Department of Health and Senior Services will provide you with information.

Adapted from CDC. *Anthrax: What You Need To Know*. July 31, 2003.

Center for Emergency Response/Terrorism
Missouri Department of Health & Senior Services
http://www.dhss.state.mo.us/BT_Response/BT_Response.html
December 21. 2004

Tularemia

What is tularemia?
Tularemia is an infectious disease caused by a bacterium, *Francisella tularensis*, which is found in numerous wild animals, especially rodents, rabbits, and hares. *F. tularensis* is highly infectious; a small number of bacteria (10-50 organisms) can cause disease.

How do people become infected with the tularemia bacteria?
Typically, persons become infected through the bites of arthropods (most commonly, ticks and deerflies) that have fed on an infected animal, by handling infected animal carcasses, by eating or drinking contaminated food or water, or by inhaling infected aerosols. Note that persons with tularemia have not been known to transmit the infection to others, so infected persons do not need to be isolated.

There is concern that tularemia bacteria might be used by terrorists, who would likely disseminate the organisms through the air in the form of an aerosol, resulting in cases of inhalational tularemia. Persons with inhalational tularemia generally experience severe respiratory illness, including life-threatening pneumonia and systemic infection, if they are not treated.

Does tularemia occur naturally in the United States?
Yes. It is a widespread disease of animals. Approximately 200 cases of tularemia in humans are reported annually in the United States, mostly in persons living in the south-central and western states (including Missouri). Nearly all cases occur in rural areas and are associated with the bites of infectious ticks and biting flies, or with the handling of infected rodents, rabbits, or hares.

What are the signs and symptoms of tularemia?
Depending on the route of exposure, infection with *F. tularensis* may result in skin ulcers, swollen and painful lymph glands, inflamed eyes, sore throat, oral ulcers, or pneumonia. If the bacteria are inhaled, symptoms can include the abrupt onset of fever, chills, headache, muscle aches, joint pain, dry cough, and progressive weakness. Persons with pneumonia can develop chest pain, difficulty breathing, bloody sputum, and respiratory failure, and 40% or more of persons with the lung and systemic forms of tularemia may die if they are not treated with appropriate antibiotics.

The time from initial infection until the appearance of symptoms is typically 3-5 days, with a range of 1-14 days.

How is tularemia diagnosed?
When tularemia is suspected based on the patient's history and physical examination, specimens such as blood or sputum will be collected and tested for evidence of tularemia infection (and other potential infections) in a medical laboratory.

Can tularemia be treated?
Yes, tularemia can be treated effectively with antibiotics. As with any infection, early diagnosis is important.

If a person is thought to have been exposed to the tularemia bacteria, what can be done?
If an individual is believed to have been very recently exposed to *F. tularensis*, treatment with antibiotics for 14 days may be recommended as a means of preventing disease.

Is there a vaccine available for tularemia?
A tularemia vaccine is currently under review by the Food and Drug Administration (FDA).

What should I do if cases of tularemia start to occur in my community?
Local and state public health officials will provide you with the information you will need. Adapted from CDC. *Frequently Asked Questions (FAQ) About Tularemia*. July 2, 2003.

Plague

What is plague?
Plague is a serious disease caused by *Yersinia pestis* (*Y. pestis*), a bacteria found in rodents and their fleas in many areas around the world. Two forms of the disease are bubonic plague and pneumonic plague. Approximately 5-15 naturally occurring cases occur each year in the western United States, and are readily controlled by standard public health measures. Most of these cases are the bubonic form of the disease.

What is the difference between bubonic plague and pneumonic plague?
Bubonic plague is transmitted through the bite of an infected flea, or through exposure to infectious material through a break in the skin. Bubonic plague cannot be transmitted from person to person.

Pneumonic plague is transmitted when a person breathes in *Y. pestis* particles in the air, resulting in infection of the lungs. Pneumonic plague can be transmitted from person to person through close (within 6 feet) contact with a person (or animal) who has pneumonic plague. Pneumonic plague could also result from breathing in *Y. pestis* particles released into the air by a terrorist. Someone exposed to *Y. pestis* through the air—either from close, direct exposure to a person or animal with plague pneumonia or from an intentional aerosol release—would become ill within 1-6 days.

Symptoms of bubonic plague include fever, chills, and swollen, tender lymph glands called buboes.

Symptoms of pneumonic plague include fever, weakness, and pneumonia with shortness of breath, chest pain, cough, and sometimes bloody or watery sputum. Nausea, vomiting, and abdominal pain may also occur. Without early treatment, there is usually respiratory failure, shock, and rapid death.

Can plague be treated?
Yes. Several types of antibiotics are effective for treating plague, but they must be started early in the course of the disease.

Can a person exposed to plague bacteria avoid becoming sick?
Yes. People who have had close contact with a person who has pneumonic plague, or who has been exposed to aerosolized *Y. pestis*, can greatly reduce the chance of becoming sick if they begin antibiotic treatment soon after exposure. Treatment consists of taking antibiotics for 7 days.

Is a vaccine available to prevent pneumonic plague?
Currently, no plague vaccine is available in the United States.

Why are we concerned about plague as a bioweapon that could be used by terrorists?
Y. pestis used in an aerosol attack could cause cases of the pneumonic form of plague. About 1-6 days after becoming infected, people would develop pneumonic plague, and then could spread the disease to others who have close contact with them. Because of the delay between being exposed to the bacteria and becoming sick, people could travel over a large area before becoming contagious and potentially infecting others.

How long can plague bacteria exist in the environment?
Y. pestis is easily destroyed by sunlight and drying. When released into air, it can survive for up to 1 hour.

What should I do if I think I have plague?
If you are showing symptoms of plague infection, call your health-care provider right away.

What should I do if cases of plague start to occur in my community?
Your local health department and the Missouri Department of Health and Senior Services will provide you with information.

Adapted from CDC. *Frequently Asked Questions (FAQ) About Plague*. October 3, 2002.

Important Information for Persons Taking Ciprofloxacin as Preventive Treatment for Anthrax

If you have been given **ciprofloxacin** as preventive treatment for anthrax and you are also currently taking **one or more of the following drugs**, it is very important that you take the appropriate actions described in this table.

Your Current Drug	Actions to Take
• **acrosoxacin or rosoxacin (Eradacil)** • **cinoxacin (Cinobac)** • **ciprofloxacin (Cipro, Ciloxan)** • **gatafloxacin (Tequin)** • **grepafloxacin (Raxar)** • **levafloxacin (Levaquin, Quixin)** • **lomefloxacin (Maxaquin)** • **moxifloxacin (Avelox, ABC Pak)** • **nadifloxacin (Acuatim)** • **norfloxacin (Chibroxin, Noroxin)** • **nalidixic acid (NegGram)** • **ofloxacin (Floxin, Ocuflox)** • **oxolinic acid; pefloxacin (Peflacine)** • **rufloxacin** • **sparfloxacin (Zagam, Respipac)** • **temafloxacin** • **trovafloxacin or alatrofloxacin (Trovan)**	Stop taking your current drug. Contact your physician or other medical provider for further instructions. While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **theophylline (Theo-Dur, Slo-BID, Slo-Phyllin, Uniphyl)** • **aminophylline** • **oxtriphylline (Choledyl SA)**	Decrease the dose of your current drug by 50% (that is, take half as much of the drug as you have been taking). Contact your physician or other medical provider for further instructions. While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **probenecid (Benemid)**	Stop taking the probenecid (Benemid). Contact your physician or other medical provider for further instructions. While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **warfarin (Coumadin)**	Begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for possible further instructions regarding the warfarin (Coumadin).

If you are taking other drugs not listed here, continue to take them in addition to taking the ciprofloxacin exactly as prescribed. See page 3 for more information.

If you have kidney disease or a condition that causes a decrease in your kidney function, begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for further instructions.

If you have epilepsy or seizures, begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for further instructions.

Additional information is presented on the next two pages. It is very important that you read all three pages of this document and follow the instructions provided.

PATIENT INFORMATION: CIPROFLOXACIN 500 MG TABLET

This drug belongs to a class of drugs called quinolone antibiotics. You have been given this drug for protection against possible exposure to infection-causing bacteria. This drug prevents: **Anthrax**

You have been provided a limited supply of medicine. Public health officials will inform you if you need more medicine after you finish this supply. If so, you will be told how to get more medicine. You will be told if no more medicine is needed. You may also be switched from this medicine to a different medicine based on laboratory tests. Since anthrax can develop quickly and be life threatening, it is very important that you complete the full course of therapy recommended by public health officials.

DOSING INSTRUCTIONS: Take one tablet by mouth, two times a day unless otherwise prescribed.

- You will be provided special dosing instructions for children.
- Keep taking your medicine, even if you feel okay, unless your doctor tells you to stop. If you stop taking this medicine to soon, you may become ill.
- You should take this medicine with a full glass of water. Drink several glasses of water each day while you are taking this medicine. It is best to take this medicine 2 hours after a meal. If it upsets your stomach, you may take it with food, but do not take it with dairy products such as milk, yogurt, or cheese.
- If you miss a dose, take the missed dose as soon as possible. If it is almost time for your next regular dose, wait until then to take your medicine, and skip the missed dose. Do not take two doses at the same time.
- This medication has been prescribed for your current condition only. Do not use it later for another infection or give it to someone else.

WARNINGS:

- Do not take this medicine if you have had an allergic reaction to ciprofloxacin or other quinolone medicines such as gatafloxacin (Tequin®), levofloxacin (Levaquin®), norfloxacin (Noroxin®), ofloxacin (Floxin®) or nalidixic acid (NegGram®).
- Until information is obtained about which drug is most effective against anthrax, medical experts from the Centers for Disease Control and Prevention and the American College of Obstetricians and Gynecologists, recommend children and pregnant and breast-feeding women receive ciprofloxacin to prevent the life-threatening complications of anthrax. If you are currently breast-feeding and have concerns about exposing your baby to ciprofloxacin, you may consider discarding the breast milk until you have finished the medication.
- This medicine may make you dizzy or lightheaded. Avoid driving or using machinery until you know how it will affect you.
- This medicine increases the chance of sunburn; avoid prolonged exposure to sunlight or tanning equipment. If you have to be in the sun, make sure to use sunscreen (SPF 15 or greater) to protect your skin.

ADVERSE REACTIONS: Stop taking ciprofloxacin and call your doctor or seek medical attention right away by visiting an emergency room if you are having any of these side effects: rash or hives; swelling of face, throat, or lips; shortness of breath or trouble breathing; seizures; or severe diarrhea.

SIDE EFFECTS: Rare side effects may occur that usually do not need medical attention. These side effects may go away while your body adjusts to the medicine. These side effects include nausea, mild diarrhea, stomach pain, dizziness, and headache. If you experience diarrhea, consider adding yogurt or lactobacillus to your diet. A re-hydration solution such as Pedialyte® is helpful if you have severe diarrhea. Talk with your doctor if any of these side effects become bothersome.

FOOD INTERACTIONS: Avoid drinking more than one or two caffeinated beverages (coffee, tea, soft drinks) per day.[1,2] Avoid taking this medicine within 2 hours of dairy products containing large amounts of calcium such as milk, yogurt, or cheese. [1,2]

DRUG INTERACTIONS:

This section provides information in addition to that contained on page 1. Be sure you have also read the instructions on page 1.

Take the following drugs 2 hours after or 6 hours before ciprofloxacin:

Antacids (Maalox®, Mylanta®)[1,2]
Calcium supplements (Oscal®)[1]
Didanosine (Videx®)[1,2]
Iron supplements (Vitron-C®, Feosol®)[1,2]
Sucralfate (Carafate®)[1,2]
Vitamins with mineral supplements (Centrum®, Theragran-M®)
Zinc supplements[1,2]

Consult a health care professional within 3-5 days after starting ciprofloxacin for monitoring and possible dosage change if you are taking one of the following medications:

Cyclosporine (Neoral®)[2]
Foscarnet (Foscavir®)[2]
Fosphenytoin (Cerebyx®)[1,2]
Mexiletine (Mexitil®)[2]
Phenytoin (Dilantin®)[1,2]

You may experience more side effects from the following medications when taken with ciprofloxacin. Please consult your health care professional.

Caffeine (Vivarin®)[1,2]
Clozapine (Clozaril®)[2]
Diazepam (Valium®)[2]
Glyburide (Diabeta®)[1]
Methadone (Dolophine®)[2]
Metoprolol (Lopressor®)[1,2]
Propranolol (Inderal®)[1]
Olanzapine (Zyprexa®)[1,2]
Ropinirole (Requip®)[1]

Oral corticosteroids such as cortisone, hydrocortisone, prednisolone, prednisone, methylprednisolone, triamcinolone, dexamethasone, betamethasone may increase your risk for tendon rupture. Use precaution when exercising and report any tendon pain or inflammation. [1]

HERBAL INTERACTIONS: Do not take fennel or dandelion within 2 hours of taking ciprofloxacin. You may take them 2 hours after or 6 hours before ciprofloxacin.[1]

STORAGE:
Keep this medicine out of the reach of children.
Store away from heat and direct light.
Ciprofloxacin oral suspension may be refrigerated. However, keep this medicine from freezing.
Do not store this medicine in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause this medicine to not work.
Keep this medicine from freezing.

REFERENCES:

1. DRUG-REAX Interactive Drug Interactions; MICROMEDEX Healthcare Series, 2002.
2. Drug Interaction Facts; Facts and Comparisons, 2002.

Health Department Hotline: 800-XXX-XXXX (Fill in your toll free hotline number)

Important Information for Persons Taking Doxycycline as Preventive Treatment for Anthrax

If you have been given **doxycycline** as preventive treatment for anthrax and you are also currently taking **one or more of the following drugs**, it is very important that you take the appropriate actions described in this table.

Your Current Drug	Actions to Take
• **demeclocycline (Declomycin)** • **doxycycline (Adoxa, Bio-Tab, Doryx, Doxy, Monodox, Periostat, Vibra-Tabs, Vibramycin)** • **minocycline (Arestin, Dynacin, Minocin, Vectrin)** • **oxytetracycline (Terak, Terra-Cortril, Terramycin, Urobiotic-250)** • **tetracycline (Achromycin V, Sumycin, Topicycline, Helidac)**	**Stop taking your current drug. Contact your physician or other medical provider for further instructions.** While you are doing this, continue to take the doxycycline exactly as prescribed unless your physician or other medical provider tells you differently.
• **warfarin (Coumadin)**	Begin taking the doxycycline exactly as prescribed and contact your physician or other medical provider for further instructions regarding the warfarin (Coumadin).
• **birth control pills (oral contraceptives)**	**Birth control pills (oral contraceptives) containing estrogen may not work properly if you take them while you are taking doxycycline. Unplanned pregnancies may occur. You should use a different or additional means of birth control while you are taking doxycycline.** Continue to take the doxycycline exactly as prescribed unless your physician or other medical provider tells you differently.

If you are taking other drugs not listed here, continue to take them in addition to taking the doxycycline exactly as prescribed. See page 3 for more information.

If you have liver disease or a condition that causes a decrease in your liver function, begin taking the doxycycline exactly as prescribed and contact your physician or other medical provider for further instructions.

Additional information is presented on the next two pages. It is very important that you read all three pages of this document and follow the instructions provided.

PATIENT INFORMATION: DOXYCYCLINE 100 MG TABLET

This drug belongs to a class of drugs called tetracycline antibiotics. You have been given this drug for protection against possible exposure to infection-causing bacteria. This drug prevents: **Anthrax**

You have been provided a limited supply of medicine. Public health officials will inform you if you need more medicine after you finish this supply. If so, upon your follow-up visit, you will be told how to get more medicine. You will be told if no more medicine is needed. You may also be switched from this medicine to a different medicine based on laboratory tests. Since anthrax can develop quickly and be life threatening, it is very important that you complete the full course of therapy recommended by public health officials.

DOSING INSTRUCTIONS: Take one tablet by mouth, two times a day unless otherwise prescribed.

- Keep taking your medicine, even if you feel okay, unless your healthcare provider tells you to stop. If you stop taking this medicine to soon, you may become ill.
- You may take your medicine with or without food or milk, but food or milk may help you avoid stomach upset.
- If you miss a dose, take the missed dose as soon as possible. If it is almost time for your next regular dose, wait until then to take your medicine, and skip the missed dose. Do not take two doses at the same time.
- This medication has been prescribed for your current condition only. Do not use it later for another infection or give it to someone else.

WARNINGS:

- Do not take this medicine if you have had an allergic reaction to any tetracycline antibiotics such as demeclocycline, doxycycline, minocycline, or oxytetracycline.
- This medicine increases the chance of sunburn; avoid prolonged exposure to sunlight or tanning equipment. If you have to be in the sun, make sure to use sunscreen (SPF 15 or greater) to protect your skin.
- Women may have vaginal yeast infections from taking this medicine. An over-the-counter vaginal, antifungal product will help this problem.

ADVERSE REACTIONS: Stop taking doxycycline and call your doctor or seek medical attention right away by visiting an emergency room if you are having any of these side effects: skin rash, hives, or itching; wheezing or trouble breathing; swelling of the face, lips, or throat.

SIDE EFFECTS: Rare side effects may occur that usually do not need medical attention. These side effects may go away while your body adjusts to the medicine. These side effects include diarrhea, upset stomach, nausea, sore mouth or throat, sensitivity to sunlight, or itching of the mouth or vagina lasting more than 2 days. If you experience diarrhea, consider adding yogurt or lactobacillus to your diet. A re-hydration solution such as Pedialyte® is helpful if you have severe diarrhea. Talk with your doctor if any of these side effects become bothersome.

DRUG INTERACTIONS:

This section provides information in addition to that contained on page 1. Be sure you have also read the instructions on page 1.

The following medications and over-the-counter products should be taken three hours before or two hours after taking doxycycline:

Antacids (Maalox®, Mylanta®)[1,2]
Bismuth subsalicylate (Pepto-Bismol®)[1,2]
Calcium supplements (Oscal®)[1]
Choline and magnesium salicyclates combination (Trilisate®)
Cholestyramine (Questran®)
Colestipol (Colestid®)[2]
Iron supplements (Vitron-C®, Feosol®)[1,2]
Potassium Citrate (Urocit-K®)[2]
Magnesium-containing products (Mag-Ox®, Milk of Magnesia) [1,2]
Sodium bicarbonate (baking soda) [2]
Vitamin preparations that contain minerals (Centrum®, Theragran-M®)

Doxycycline may affect the following medications. Consult your doctor within 3-5 days if you are currently taking any of the following medications:

Digoxin (Lanoxin®)[2]
Dicumarol[1]
Insulin (Humulin®, Novolin®)[2]
Isotretinoin (Accutane®)[1]
Methoxyflurane (Penthrane®)[2]
Methotrexate[1,2]
Theophylline (Theo-Dur®)[2]

Oral contraceptives (birth control pills) containing estrogen may not work properly if you take them while you are taking this medicine. Unplanned pregnancies may occur. You should use a different or additional means of birth control while you are taking this medication. If you have questions about this, consult your doctor or pharmacist.[1,2]

The following medications may decrease the amount of doxycycline in your body. Consult your doctor whether you need to receive a higher dose of doxycycline:

Carbamazepine (Tegretol®)[1,2]
Fosphenytoin (Cerebyx®)[1]
Phenobarbital[1,2]
Phenytoin (Dilantin®)[1,2]
Rifabutin (Mycobutin®)[2]
Rifampin (Rifadin®)[1,2]

HERBAL INTERACTIONS: The herbal supplements, St John's Wort and Dong Quai, should be avoided when taking doxycycline.

STORAGE:

- Keep this medicine out of the reach of children.
- Store away from heat and direct light.
- Do not store this medicine in the bathroom, near the kitchen sink, or in other damp places.
- Heat or moisture may cause this medicine to not work.
- Keep this medicine from freezing.

REFERENCES:

1. DRUG-REAX Interactive Drug Interactions; *MICROMEDEX Healthcare Series*, 2002.
2. Drug Interaction Facts; *Facts and Comparisons*, 2002.

Health Department Hotline: 800-XXX-XXX (Fill in your agency hotline number)

Important Information for Persons Taking Ciprofloxacin as Preventive Treatment for Plague

If you have been given **ciprofloxacin** as preventive treatment for plague and you are also currently taking **one or more of the following drugs**, it is very important that you take the appropriate actions described in this table.

Your Current Drug	Actions to Take
• **acrosoxacin or rosoxacin (Eradacil)** • **cinoxacin (Cinobac)** • **ciprofloxacin (Cipro, Ciloxan)** • **gatafloxacin (Tequin)** • **grepafloxacin (Raxar)** • **levafloxacin (Levaquin, Quixin)** • **lomefloxacin (Maxaquin)** • **moxifloxacin (Avelox, ABC Pak)** • **nadifloxacin (Acuatim)** • **norfloxacin (Chibroxin, Noroxin)** • **nalidixic acid (NegGram)** • **ofloxacin (Floxin, Ocuflox)** • **oxolinic acid; pefloxacin (Peflacine)** • **rufloxacin** • **sparfloxacin (Zagam, Respipac)** • **temafloxacin** • **trovafloxacin or alatrofloxacin (Trovan)**	**Stop taking your current drug. Contact your physician or other medical provider for further instructions.** While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **theophylline (Theo-Dur, Slo-BID, Slo-Phyllin, Uniphyl)** • **aminophylline** • **oxtriphylline (Choledyl SA)**	Decrease the dose of your current drug by 50% (that is, take half as much of the drug as you have been taking). Contact your physician or other medical provider for further instructions. While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **probenecid (Benemid)**	**Stop taking the probenecid (Benemid). Contact your physician or other medical provider for further instructions.** While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **warfarin (Coumadin)**	Begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for possible further instructions regarding the warfarin (Coumadin).

If you are taking other drugs not listed here, continue to take them in addition to taking the ciprofloxacin exactly as prescribed. See page 3 for more information.

If you have kidney disease or a condition that causes a decrease in your kidney function, begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for further instructions.

If you have epilepsy or seizures, begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for further instructions.

Additional information is presented on the next two pages. It is very important that you read all three pages of this document and follow the instructions provided.

PATIENT INFORMATION: CIPROFLOXACIN 500 MG TABLET

This drug belongs to a class of drugs called quinolone antibiotics. You have been given this drug for protection against possible exposure to infection-causing bacteria. This drug prevents: **Plague**

It is very important that you take this medicine as prescribed for 7 days. After you have completed this 7-day course of treatment, discard all remaining medicine.

Since plague can develop quickly and be life threatening, it is very important that you complete the full course of therapy recommended by public health officials.

DOSING INSTRUCTIONS: Take one tablet by mouth, two times a day unless otherwise prescribed.

- You will be provided special dosing instructions for children.
- Keep taking your medicine, even if you feel okay, unless your doctor tells you to stop. If you stop taking this medicine to soon, you may become ill.
- You should take this medicine with a full glass of water. Drink several glasses of water each day while you are taking this medicine. It is best to take this medicine 2 hours after a meal. If it upsets your stomach, you may take it with food, but do not take it with dairy products such as milk, yogurt, or cheese.
- If you miss a dose, take the missed dose as soon as possible. If it is almost time for your next regular dose, wait until then to take your medicine, and skip the missed dose. Do not take two doses at the same time.
- This medication has been prescribed for your current condition only. Do not use it later for another infection or give it to someone else.

WARNINGS:

- Do not take this medicine if you have had an allergic reaction to ciprofloxacin or other quinolone medicines such as gatafloxacin (Tequin®), levofloxacin (Levaquin®), norfloxacin (Noroxin®), ofloxacin (Floxin®) or nalidixic acid (NegGram®).
- If you are currently breast-feeding and have concerns about exposing your baby to ciprofloxacin, you may consider discarding the breast milk until you have finished the medication.
- This medicine may make you dizzy or lightheaded. Avoid driving or using machinery until you know how it will affect you.
- This medicine increases the chance of sunburn; avoid prolonged exposure to sunlight or tanning equipment. If you have to be in the sun, make sure to use sunscreen (SPF 15 or greater) to protect your skin.

ADVERSE REACTIONS: Stop taking ciprofloxacin and call your doctor or seek medical attention right away by visiting an emergency room if you are having any of these side effects: rash or hives; swelling of face, throat, or lips; shortness of breath or trouble breathing; seizures; or severe diarrhea.

SIDE EFFECTS: Rare side effects may occur that usually do not need medical attention. These side effects may go away while your body adjusts to the medicine. These side effects include nausea, mild diarrhea, stomach pain, dizziness, and headache. If you experience diarrhea, consider adding yogurt or lactobacillus to your diet. A re-hydration solution such as Pedialyte® is helpful if you have severe diarrhea. Talk with your doctor if any of these side effects become bothersome.

FOOD INTERACTIONS: Avoid drinking more than one or two caffeinated beverages (coffee, tea, soft drinks) per day.[1,2] Avoid taking this medicine within 2 hours of dairy products containing large amounts of calcium such as milk, yogurt, or cheese. [1,2]

DRUG INTERACTIONS:

This section provides information in addition to that contained on page 1. Be sure you have also read the instructions on page 1.

Take the following drugs 2 hours after or 6 hours before ciprofloxacin:

Antacids (Maalox®, Mylanta®)[1,2]
Calcium supplements (Oscal®)[1]
Didanosine (Videx®)[1,2]
Iron supplements (Vitron-C®, Feosol®)[1,2]
Sucralfate (Carafate®)[1,2]
Vitamins with mineral supplements (Centrum®, Theragran-M®)
Zinc supplements[1,2]

Consult a health care professional within 3-5 days after starting ciprofloxacin for monitoring and possible dosage change if you are taking one of the following medications:

Cyclosporine (Neoral®)[2]
Foscarnet (Foscavir®)[2]
Fosphenytoin (Cerebyx®)[1,2]
Mexiletine (Mexitil®)[2]
Phenytoin (Dilantin®)[1,2]

You may experience more side effects from the following medications when taken with ciprofloxacin. Please consult your health care professional.

Caffeine (Vivarin®)[1,2]
Clozapine (Clozaril®)[2]
Diazepam (Valium®)[2]
Glyburide (Diabeta®)[1]
Methadone (Dolophine®)[2]
Metoprolol (Lopressor®)[1,2]
Propranolol (Inderal®)[1]
Olanzapine (Zyprexa®)[1,2]
Ropinirole (Requip®)[1]

Oral corticosteroids such as cortisone, hydrocortisone, prednisolone, prednisone, methylprednisolone, triamcinolone, dexamethasone, betamethasone may increase your risk for tendon rupture. Use precaution when exercising and report any tendon pain or inflammation.[1]

HERBAL INTERACTIONS: Do not take fennel or dandelion within 2 hours of taking ciprofloxacin. You may take them 2 hours after or 6 hours before ciprofloxacin.[1]

STORAGE:
Keep this medicine out of the reach of children.
Store away from heat and direct light.
Ciprofloxacin oral suspension may be refrigerated. However, keep this medicine from freezing.
Do not store this medicine in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause this medicine to not work.
Keep this medicine from freezing.

REFERENCES:

3. DRUG-REAX Interactive Drug Interactions; MICROMEDEX Healthcare Series, 2002.
4. Drug Interaction Facts; Facts and Comparisons, 2002.

Health Department Hotline: 800-XXX-XXXX (Fill in your agency hotline number)

Important Information for Persons Taking Doxycycline as Preventive Treatment for Plague

If you have been given **doxycycline** as preventive treatment for plague and you are also currently taking **one or more of the following drugs**, it is very important that you take the appropriate actions described in this table.

Your Current Drug	Actions to Take
• **demeclocycline (Declomycin)** • **doxycycline (Adoxa, Bio-Tab, Doryx, Doxy, Monodox, Periostat, Vibra-Tabs, Vibramycin)** • **minocycline (Arestin, Dynacin, Minocin, Vectrin)** • **oxytetracycline (Terak, Terra-Cortril, Terramycin, Urobiotic-250)** • **tetracycline (Achromycin V, Sumycin, Topicycline, Helidac)**	**Stop taking your current drug. Contact your physician or other medical provider for further instructions.** While you are doing this, continue to take the doxycycline exactly as prescribed unless your physician or other medical provider tells you differently.
• **warfarin (Coumadin)**	Begin taking the doxycycline exactly as prescribed and contact your physician or other medical provider for further instructions regarding the warfarin (Coumadin).
• **birth control pills (oral contraceptives)**	**Birth control pills (oral contraceptives) containing estrogen may not work properly if you take them while you are taking doxycycline. Unplanned pregnancies may occur. You should use a different or additional means of birth control while you are taking doxycycline.** Continue to take the doxycycline exactly as prescribed unless your physician or other medical provider tells you differently.

If you are taking other drugs not listed here, continue to take them in addition to taking the doxycycline exactly as prescribed. See page 3 for more information.

If you have liver disease or a condition that causes a decrease in your liver function, begin taking the doxycycline exactly as prescribed and contact your physician or other medical provider for further instructions.

Additional information is presented on the next two pages. It is very important that you read all three pages of this document and follow the instructions provided.

PATIENT INFORMATION: DOXYCYCLINE 100 MG TABLET

This drug belongs to a class of drugs called tetracycline antibiotics. You have been given this drug for protection against possible exposure to infection-causing bacteria. This drug prevents: **Plague**

It is very important that you take this medicine as prescribed for 7 days. After you have completed this 7-day course of treatment, discard all remaining medicine.

Since plague can develop quickly and be life threatening, it is very important that you complete the full course of therapy recommended by public health officials.

DOSING INSTRUCTIONS: Take one tablet by mouth, two times a day unless otherwise prescribed.

- Keep taking your medicine, even if you feel okay, unless your healthcare provider tells you to stop. If you stop taking this medicine to soon, you may become ill.
- You may take your medicine with or without food or milk, but food or milk may help you avoid stomach upset.
- If you miss a dose, take the missed dose as soon as possible. If it is almost time for your next regular dose, wait until then to take your medicine, and skip the missed dose. Do not take two doses at the same time.
- This medication has been prescribed for your current condition only. Do not use it later for another infection or give it to someone else.

WARNINGS:

- Do not take this medicine if you have had an allergic reaction to any tetracycline antibiotics such as demeclocycline, doxycycline, minocycline, or oxytetracycline.
- This medicine increases the chance of sunburn; avoid prolonged exposure to sunlight or tanning equipment. If you have to be in the sun, make sure to use sunscreen (SPF 15 or greater) to protect your skin.
- Women may have vaginal yeast infections from taking this medicine. An over-the-counter vaginal, antifungal product will help this problem.

ADVERSE REACTIONS: Stop taking doxycycline and call your doctor or seek medical attention right away by visiting an emergency room if you are having any of these side effects: skin rash, hives, or itching; wheezing or trouble breathing; swelling of the face, lips, or throat.

SIDE EFFECTS: Rare side effects may occur that usually do not need medical attention. These side effects may go away while your body adjusts to the medicine. These side effects include diarrhea, upset stomach, nausea, sore mouth or throat, sensitivity to sunlight, or itching of the mouth or vagina lasting more than 2 days. If you experience diarrhea, consider adding yogurt or lactobacillus to your diet. A re-hydration solution such as Pedialyte® is helpful if you have severe diarrhea. Talk with your doctor if any of these side effects become bothersome.

DRUG INTERACTIONS:

This section provides information in addition to that contained on page 1. Be sure you have also read the instructions on page 1.

The following medications and over-the-counter products should be taken three hours before or two hours after taking doxycycline:

Antacids (Maalox®, Mylanta®)[1,2]
Bismuth subsalicylate (Pepto-Bismol®)[1,2]
Calcium supplements (Oscal®)[1]
Choline and magnesium salicylates combination (Trilisate®)
Cholestyramine (Questran®)
Colestipol (Colestid®)[2]
Iron supplements (Vitron-C®, Feosol®)[1,2]
Potassium Citrate (Urocit-K®)[2]
Magnesium-containing products (Mag-Ox®, Milk of Magnesia) [1,2]
Sodium bicarbonate (baking soda) [2]
Vitamin preparations that contain minerals (Centrum®, Theragran-M®)

Doxycycline may affect the following medications. Consult your doctor within 3-5 days if you are currently taking any of the following medications:

Digoxin (Lanoxin®)[2]
Dicumarol[1]
Insulin (Humulin®, Novolin®)[2]
Isotretinoin (Accutane®)[1]
Methoxyflurane (Penthrane®)[2]
Methotrexate[1,2]
Theophylline (Theo-Dur®)[2]

Oral contraceptives (birth control pills) containing estrogen may not work properly if you take them while you are taking this medicine. Unplanned pregnancies may occur. You should use a different or additional means of birth control while you are taking this medication. If you have questions about this, consult your doctor or pharmacist.[1,2]

The following medications may decrease the amount of doxycycline in your body. Consult your doctor whether you need to receive a higher dose of doxycycline:

Carbamazepine (Tegretol®)[1,2]
Fosphenytoin (Cerebyx®)[1]
Phenobarbital[1,2]
Phenytoin (Dilantin®)[1,2]
Rifabutin (Mycobutin®)[2]
Rifampin (Rifadin®)[1,2]

HERBAL INTERACTIONS: The herbal supplements, St John's Wort and Dong Quai, should be avoided when taking doxycycline.

STORAGE:

- Keep this medicine out of the reach of children.
- Store away from heat and direct light.
- Do not store this medicine in the bathroom, near the kitchen sink, or in other damp places.
- Heat or moisture may cause this medicine to not work.
- Keep this medicine from freezing.

REFERENCES:

3. DRUG-REAX Interactive Drug Interactions; *MICROMEDEX Healthcare Series*, 2002.
4. Drug Interaction Facts; *Facts and Comparisons*, 2002.

Health Department Hotline: 800-XXX-XXX (Fill in your agency hotline number)

Important Information for Persons Taking Ciprofloxacin as Preventive Treatment for Tularemia

If you have been given **ciprofloxacin** as preventive treatment for tularemia and you are also currently taking **one or more of the following drugs**, it is very important that you take the appropriate actions described in this table.

Your Current Drug	Actions to Take
• **acrosoxacin or rosoxacin (Eradacil)** • **cinoxacin (Cinobac)** • **ciprofloxacin (Cipro, Ciloxan)** • **gatafloxacin (Tequin)** • **grepafloxacin (Raxar)** • **levafloxacin (Levaquin, Quixin)** • **lomefloxacin (Maxaquin)** • **moxifloxacin (Avelox, ABC Pak)** • **nadifloxacin (Acuatim)** • **norfloxacin (Chibroxin, Noroxin)** • **nalidixic acid (NegGram)** • **ofloxacin (Floxin, Ocuflox)** • **oxolinic acid; pefloxacin (Peflacine)** • **rufloxacin** • **sparfloxacin (Zagam, Respipac)** • **temafloxacin** • **trovafloxacin or alatrofloxacin (Trovan)**	**Stop taking your current drug. Contact your physician or other medical provider for further instructions.** While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **theophylline (Theo-Dur, Slo-BID, Slo-Phyllin, Uniphyl)** • **aminophylline** • **oxtriphylline (Choledyl SA)**	Decrease the dose of your current drug by 50% (that is, take half as much of the drug as you have been taking). Contact your physician or other medical provider for further instructions. While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **probenecid (Benemid)**	Stop taking the probenecid (Benemid). Contact your physician or other medical provider for further instructions. While you are doing this, continue to take the ciprofloxacin exactly as prescribed unless your physician or other medical provider tells you differently.
• **warfarin (Coumadin)**	Begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for possible further instructions regarding the warfarin (Coumadin).

If you are taking other drugs not listed here, continue to take them in addition to taking the ciprofloxacin exactly as prescribed. See page 3 for more information.

If you have kidney disease or a condition that causes a decrease in your kidney function, begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for further instructions.

If you have epilepsy or seizures, begin taking the ciprofloxacin exactly as prescribed and contact your physician or other medical provider for further instructions.

Additional information is presented on the next two pages. It is very important that you read all three pages of this document and follow the instructions provided.

PATIENT INFORMATION: CIPROFLOXACIN 500 MG TABLET

This drug belongs to a class of drugs called quinolone antibiotics. You have been given this drug for protection against possible exposure to infection-causing bacteria. This drug prevents: **Tularemia**

Since tularemia can be life threatening, it is very important that you complete the full course of therapy recommended by public health officials.

DOSING INSTRUCTIONS: Take one tablet by mouth, two times a day unless otherwise prescribed.

- You will be provided special dosing instructions for children.
- Keep taking your medicine, even if you feel okay, unless your doctor tells you to stop. If you stop taking this medicine to soon, you may become ill.
- You should take this medicine with a full glass of water. Drink several glasses of water each day while you are taking this medicine. It is best to take this medicine 2 hours after a meal. If it upsets your stomach, you may take it with food, but do not take it with dairy products such as milk, yogurt, or cheese.
- If you miss a dose, take the missed dose as soon as possible. If it is almost time for your next regular dose, wait until then to take your medicine, and skip the missed dose. Do not take two doses at the same time.
- This medication has been prescribed for your current condition only. Do not use it later for another infection or give it to someone else.

WARNINGS:

- Do not take this medicine if you have had an allergic reaction to ciprofloxacin or other quinolone medicines such as gatafloxacin (Tequin®), levofloxacin (Levaquin®), norfloxacin (® ® c acid (NegGram®).
- If you are currently breast-feeding and have concerns about exposing your baby to ciprofloxacin, you may consider discarding the breast milk until you have finished the medication.
- This medicine may make you dizzy or lightheaded. Avoid driving or using machinery until you know how it will affect you.
- This medicine increases the chance of sunburn; avoid prolonged exposure to sunlight or tanning equipment. If you have to be in the sun, make sure to use sunscreen (SPF 15 or greater) to protect your skin.

ADVERSE REACTIONS: Stop taking ciprofloxacin and call your doctor or seek medical attention right away by visiting an emergency room if you are having any of these side effects: rash or hives; swelling of face, throat, or lips; shortness of breath or trouble breathing; seizures; or severe diarrhea.

SIDE EFFECTS: Rare side effects may occur that usually do not need medical attention. These side effects may go away while your body adjusts to the medicine. These side effects include nausea, mild diarrhea, stomach pain, dizziness, and headache. If you experience diarrhea, consider adding yogurt or lactobacillus to your diet. A re-hydration solution such as Pedialyte® is helpful if you have severe diarrhea. Talk with your doctor if any of these side effects become bothersome.

FOOD INTERACTIONS: Avoid drinking more than one or two caffeinated beverages (coffee, tea, soft drinks) per day.[1,2] Avoid taking this medicine within 2 hours of dairy products containing large amounts of calcium such as milk, yogurt, or cheese. [1,2]

DRUG INTERACTIONS:

This section provides information in addition to that contained on page 1. Be sure you have also read the instructions on page 1.

Take the following drugs 2 hours after or 6 hours before ciprofloxacin:

Antacids (Maalox®, Mylanta®)[1,2]
Calcium supplements (Oscal®)[1]
Didanosine (Videx®)[1,2]
Iron supplements (Vitron-C®, Feosol®)[1,2]
Sucralfate (Carafate®)[1,2]
Vitamins with mineral supplements (Centrum®, Theragran-M®)
Zinc supplements[1,2]

Consult a health care professional within 3-5 days after starting ciprofloxacin for monitoring and possible dosage change if you are taking one of the following medications:

Cyclosporine (Neoral®)[2]
Foscarnet (Foscavir®)[2]
Fosphenytoin (Cerebyx®)[1,2]
Mexiletine (Mexitil®)[2]
Phenytoin (Dilantin®)[1,2]

You may experience more side effects from the following medications when taken with ciprofloxacin. Please consult your health care professional.

Caffeine (Vivarin®)[1,2]
Clozapine (Clozaril®)[2]
Diazepam (Valium®)[2]
Glyburide (Diabeta®)[1]
Methadone (Dolophine®)[2]
Metoprolol (Lopressor®)[1,2]
Propranolol (Inderal®)[1]
Olanzapine (Zyprexa®)[1,2]
Ropinirole (Requip®)[1]

Oral corticosteroids such as cortisone, hydrocortisone, prednisolone, prednisone, methylprednisolone, triamcinolone, dexamethasone, betamethasone may increase your risk for tendon rupture. Use precaution when exercising and report any tendon pain or inflammation. [1]

HERBAL INTERACTIONS: Do not take fennel or dandelion within 2 hours of taking ciprofloxacin. You may take them 2 hours after or 6 hours before ciprofloxacin.[1]

STORAGE:
Keep this medicine out of the reach of children.
Store away from heat and direct light.
Ciprofloxacin oral suspension may be refrigerated. However, keep this medicine from freezing.
Do not store this medicine in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause this medicine to not work.
Keep this medicine from freezing.

REFERENCES:

5. DRUG-REAX Interactive Drug Interactions; MICROMEDEX Healthcare Series, 2002.
6. Drug Interaction Facts; Facts and Comparisons, 2002.

Health Department Hotline: 800-XXX-XXXX (Fill in your agency hotline number)

Important Information for Persons Taking Doxycycline as Preventive Treatment for Tularemia

If you have been given **doxycycline** as preventive treatment for tularemia and you are also currently taking **one or more of the following drugs**, it is very important that you take the appropriate actions described in this table.

Your Current Drug	Actions to Take
• **demeclocycline (Declomycin)** • **doxycycline (Adoxa, Bio-Tab, Doryx, Doxy, Monodox, Periostat, Vibra-Tabs, Vibramycin)** • **minocycline (Arestin, Dynacin, Minocin, Vectrin)** • **oxytetracycline (Terak, Terra-Cortril, Terramycin, Urobiotic-250)** • **tetracycline (Achromycin V, Sumycin, Topicycline, Helidac)**	**Stop taking your current drug. Contact your physician or other medical provider for further instructions.** While you are doing this, continue to take the doxycycline exactly as prescribed unless your physician or other medical provider tells you differently.
• **warfarin (Coumadin)**	Begin taking the doxycycline exactly as prescribed and contact your physician or other medical provider for further instructions regarding the warfarin (Coumadin).
• **birth control pills (oral contraceptives)**	**Birth control pills (oral contraceptives) containing estrogen may not work properly if you take them while you are taking doxycycline. Unplanned pregnancies may occur. You should use a different or additional means of birth control while you are taking doxycycline.** Continue to take the doxycycline exactly as prescribed unless your physician or other medical provider tells you differently.

If you are taking other drugs not listed here, continue to take them in addition to taking the doxycycline exactly as prescribed. See page 3 for more information.

If you have liver disease or a condition that causes a decrease in your liver function, begin taking the doxycycline exactly as prescribed and contact your physician or other medical provider for further instructions.

Additional information is presented on the next two pages. It is very important that you read all three pages of this document and follow the instructions provided.

PATIENT INFORMATION: DOXYCYCLINE 100 MG TABLET

This drug belongs to a class of drugs called tetracycline antibiotics. You have been given this drug for protection against possible exposure to infection-causing bacteria. This drug prevents: **Tularemia**

Since tularemia can be life threatening, it is very important that you complete the full course of therapy recommended by public health officials.

DOSING INSTRUCTIONS: **Take one tablet by mouth, two times a day unless otherwise prescribed.**

- Keep taking your medicine, even if you feel okay, unless your healthcare provider tells you to stop. If you stop taking this medicine too soon, you may become ill.
- You may take your medicine with or without food or milk, but food or milk may help you avoid stomach upset.
- If you miss a dose, take the missed dose as soon as possible. If it is almost time for your next regular dose, wait until then to take your medicine, and skip the missed dose. Do not take two doses at the same time.
- This medication has been prescribed for your current condition only. Do not use it later for another infection or give it to someone else.

WARNINGS:

- Do not take this medicine if you have had an allergic reaction to any tetracycline antibiotics such as demeclocycline, doxycycline, minocycline, or oxytetracycline.
- This medicine increases the chance of sunburn; avoid prolonged exposure to sunlight or tanning equipment. If you have to be in the sun, make sure to use sunscreen (SPF 15 or greater) to protect your skin.
- Women may have vaginal yeast infections from taking this medicine. An over-the-counter vaginal, antifungal product will help this problem.

ADVERSE REACTIONS: Stop taking doxycycline and call your doctor or seek medical attention right away by visiting an emergency room if you are having any of these side effects: skin rash, hives, or itching; wheezing or trouble breathing; swelling of the face, lips, or throat.

SIDE EFFECTS: Rare side effects may occur that usually do not need medical attention. These side effects may go away while your body adjusts to the medicine. These side effects include diarrhea, upset stomach, nausea, sore mouth or throat, sensitivity to sunlight, or itching of the mouth or vagina lasting more than 2 days. If you experience diarrhea, consider adding yogurt or lactobacillus to your diet. A re-hydration solution such as Pedialyte® is helpful if you have severe diarrhea. Talk with your doctor if any of these side effects become bothersome.

DRUG INTERACTIONS:

This section provides information in addition to that contained on page 1. Be sure you have also read the instructions on page 1.

The following medications and over-the-counter products should be taken three hours before or two hours after taking doxycycline:

Antacids (Maalox®, Mylanta®)[1,2]
Bismuth subsalicylate (Pepto-Bismol®)[1,2]
Calcium supplements (Oscal®)[1]
Choline and magnesium salicyclates combination (Trilisate®)
Cholestyramine (Questran®)
Colestipol (Colestid®)[2]
Iron supplements (Vitron-C®, Feosol®)[1,2]
Potassium Citrate (Urocit-K®)[2]
Magnesium-containing products (Mag-Ox®, Milk of Magnesia) [1,2]
Sodium bicarbonate (baking soda) [2]
Vitamin preparations that contain minerals (Centrum®, Theragran-M®)

Doxycycline may affect the following medications. Consult your doctor within 3-5 days if you are currently taking any of the following medications:

Digoxin (Lanoxin®)[2]
Dicumarol[1]
Insulin (Humulin®, Novolin®)[2]
Isotretinoin (Accutane®)[1]
Methoxyflurane (Penthrane®)[2]
Methotrexate[1,2]
Theophylline (Theo-Dur®)[2]

Oral contraceptives (birth control pills) containing estrogen may not work properly if you take them while you are taking this medicine. Unplanned pregnancies may occur. You should use a different or additional means of birth control while you are taking this medication. If you have questions about this, consult your doctor or pharmacist.[1,2]

The following medications may decrease the amount of doxycycline in your body. Consult your doctor whether you need to receive a higher dose of doxycycline:

Carbamazepine (Tegretol®)[1,2]
Fosphenytoin (Cerebyx®)[1]
Phenobarbital[1,2]
Phenytoin (Dilantin®)[1,2]
Rifabutin (Mycobutin®)[2]
Rifampin (Rifadin®)[1,2]

HERBAL INTERACTIONS: The herbal supplements, St John's Wort and Dong Quai, should be avoided when taking doxycycline.

STORAGE:

- Keep this medicine out of the reach of children.
- Store away from heat and direct light.
- Do not store this medicine in the bathroom, near the kitchen sink, or in other damp places.
- Heat or moisture may cause this medicine to not work.
- Keep this medicine from freezing.

REFERENCES:

5. DRUG-REAX Interactive Drug Interactions; *MICROMEDEX Healthcare Series*, 2002.
6. Drug Interaction Facts; *Facts and Comparisons*, 2002.

Health Department Hotline: 800-XXX-XXX (Fill in your agency hotline number)

How to Prepare *Emergency* Dosages of Doxycycline at Home for Infants and Children

U.S. Food and Drug Administration
Center for Drug Evaluation and Research

http://www.fda.gov/cder/drug/infopage/penG_doxy/doxycyclinePeds.htm
(Important Instruction: Go to the above website, click on "Printable Card" to print the one page instruction sheet, Doxycycline for infants and children exposed to anthrax.)

Introduction

Once you have been notified by your federal, state, or local authorities that you have been exposed to anthrax, it may be necessary to prepare **emergency** doses of doxycycline for infants and children using doxycycline tablets.

The antibiotic doxycycline is used to treat anthrax and several other types of infections. Doxycycline is not generally given to children under eight years old because it can permanently discolor teeth and cause problems with tooth enamel. It may also cause delays in bone development in premature babies if taken for a long time. Bone development seems to return to normal when the medicine is stopped.

For most people, doxycycline's benefit of preventing children from becoming ill with anthrax outweighs the problems it can cause to teeth and bones. The Food and Drug Administration is providing information to caregivers who choose to give doxycycline to children who have been exposed to inhalational anthrax.

Most of the doxycycline stockpiled by the government is in tablet form. Tablets are easier to store. Some doxcycline is already stored in liquid form for infants and children but in an emergency, there may be the need to dissolve tablets into a mixture.

Bitter Pills

Children generally don't enjoy swallowing pills. FDA tried some foods and drinks to see what can mask the taste of a crushed doxycycline tablet. This document explains how to mix a crushed doxycycline tablet with food or a drink, which foods and drinks work best, and how much to give to a child.

Mixing and Dissolving Doxycycline Tablets

Doxycycline can be dissolved in water, but water does not mask the bitterness. FDA tried mixing doxycycline with the following foods and drinks:

- low fat white milk
- low fat chocolate milk

- regular (whole) chocolate milk
- chocolate pudding
- grape jelly
- strawberry jelly
- yogurt with cherry flavor
- apple juice mixed with table sugar

The following foods and drinks mixed with doxycycline generally have an acceptable taste:

- low fat white milk
- low fat chocolate milk
- regular (whole) chocolate milk
- chocolate pudding
- apple juice mixed with table sugar

The following foods mixed with doxycycline do not hide its bitterness:

- jellies
- yogurt

Here are some points to keep in mind:

- Drinks work better than soft foods like pudding or jelly to dissolve the doxcycline tablet.
- Adding sugar to apple juice will help the mixture taste better.
- Extra sugar is not needed with sweet foods like chocolate milk and pudding.
- Chocolate milk and chocolate pudding hide the taste of doxycycline better than juice.

How to mix 100 milligram (mg) Doxycycline with a food or drink

Note: To find out how much of this mixture to give a child, use the Dosing Chart below.

The following instructions should be followed using measuring spoons that measure one (1) teaspoon and one half (½) teaspoon, if they are available. If measuring spoons are not available, please use the same metal teaspoon to grind the tablet, measure the food or drink, and give the medicine. For example, if you don't have a measuring spoon to give the child one and a half (1 ½) teaspoons of the medicine mixture, use the metal teaspoon to estimate as best you can. Because the amount of fluid is so small in a one-half (1/2) teaspoon, it is better to give a little extra of the one-half (1/2) teaspoon than not enough.

You will need:

- One (1) 100-mg doxycycline tablet
- A metal teaspoon
- Measuring spoons [one (1) teaspoon; and one-half (½) teaspoon]
- 1 or 2 Small bowls
- One of these foods or drinks:
    - low fat milk
    - low fat chocolate milk
    - regular (whole) chocolate milk
    - chocolate pudding
    - apple juice mixed with table sugar*****

***If you use apple juice mixed with table sugar:**

1. Use a measuring spoon to put four (4) level teaspoons of sugar and four (4) teaspoons of apple juice in a second small bowl.
2. Stir the mixture until all the sugar is dissolved -- it may take several minutes.
3. Using the measuring spoon, add four (4) teaspoons of the juice and sugar mixture into the first bowl with the doxycycline powder from one (1) 100-mg tablet. Mix them together until the doxycycline powder dissolves.

1. Grind the doxycycline tablet into powder.

Put **one** (1) 100-mg doxycycline tablet into a small bowl and grind it into a fine powder using the back of the metal teaspoon. The powder should not have any large pieces.

2. Mix the doxycycline powder from one (1) 100-mg tablet with four (4) teaspoons of a food or drink.

Use a measuring spoon to add four (4) level ***teaspoons*** of a food or drink to the doxycycline powder in the small bowl. Mix them together until the doxycycline powder dissolves. It may be harder to dissolve the powder in pudding than in a drink.

Doses: How Much of the Doxycycline Mixture To Give A Child

Adults (and children heavier than 100 pounds) who are exposed to anthrax should take one (1) 100-mg tablet of doxycycline twice a day for 60 days (2 tablets per day).

The number of teaspoons of the doxycycline mixture to give a child depends on the child's weight. Use the chart below to see how much to give a child.

Dosing Chart for Doxycycline Mixture

- **This chart shows you the amount to give a child for one (1) dose. You should give a child two (2) doses (one in the morning and one in the evening) each day for 60 days. Use measuring spoons to measure the dose accurately.**

Oral Dosing Regimen for One Dose		
If the child weighs	**Give the child**	**which is**
0-12.5 lbs.	One half (1/2) **teaspoon** of the doxycycline mixture	12.5 mg of doxycycline
12.5 - 25 lbs.	One (1) **teaspoon** of the doxycycline mixture	25 mg of doxycycline
25 - 37.5 lbs.	One and one half (1½) **teaspoons** of the doxycycline mixture	37.5 mg of doxycycline
37.5 - 50 lbs.	Two (2) **teaspoons** of the doxycycline mixture	50 mg of doxycycline
50 - 62.5 lbs.	Two and one half (2½) **teaspoons** of the doxycycline mixture	62.5 mg of doxycycline
62.5 - 75 lbs.	Three (3) **teaspoons** of the doxycycline mixture	75 mg of doxycycline
75 - 87.5 lbs.	Three and one half (3½) **teaspoons** of the doxycycline mixture	87.5 mg of doxycycline
87.5 - 100 lbs.	Four (4) **teaspoons** of the doxycycline mixture	100 mg of doxycycline

How To Store Foods Mixed With Doxycycline

Doxycycline mixed with any of the recommended foods and drinks will keep for at least 24 hours. Store the mixture in a covered container and **always refrigerate** mixtures made with milk or pudding. Mixtures made with juice can be stored at room temperature. FDA recommends that doxycycline mixtures be prepared daily. **Unused portions should be thrown away.**

WARNINGS: If you have liver disease, contact your doctor, let him or her know you have started DOXYCYCLINE, and follow any instructions you are given.

For more information about doxycycline, go to "Doxycycline and Penicillin G Procaine for
Inhalational Anthrax (Post-Exposure)" at www.fda.gov/cder/drug/infopage/penG_doxy

A printable card in PDF format explaining how to prepare emergency dosages of doxycycline for infants and children exposed to anthrax is available from FDA at: http://www.fda.gov/cder/drug/infopage/penG_doxy/doxypeds.pdf.

Exhibit B: Medical Protocol

Mass Prophylaxis Clinic
For Dispensing Antibiotics
Guidelines for Consultation and Referral to Physician or a
Designated Health Facility for Services or Emergency Care

All individuals presenting for prophylactic treatment should be screened before they are allowed into the dispensing area. Based on the agent information below, individuals should be asked the following questions:

1. Do you have a fever?
2. Do you have a cough?
3. Do you have any chest discomfort?
4. Are you having difficulty breathing?
5. Have you recently had nausea or vomiting?
6. Do you have bloody diarrhea?
7. Have you recently experienced profound sweating for no reason?
8. Have you recently developed unexplainable sores on your body?

Individuals answering yes to any question above should be immediately escorted from the dispensing area to a clinical evaluation area. If after evaluation it is determined that the individual has clinical symptoms of a potential biological agent, he/she should be referred to their primary care physician, or transported to a designated health facility. The Physician Referral Form should be completed, one copy given to the individual to present to their physician, and a second copy retained at the dispensing site for future follow-up.

Clinical Presentations

Inhalational Anthrax. Initial phase: non-specific symptoms such as low-grade fever, nonproductive cough, headache, nausea, vomiting, malaise, fatigue, myalgias, profound sweats, chest discomfort (upper respiratory tract symptoms are rare); maybe rhonchi on chest exam, otherwise normal; chest x-ray may show mediastinal widening and/or pleural effusion; infiltrates might be present. Subsequent, fulminant phase: 1–5 days after onset of initial symptoms; may or may not be preceded by 1–3 days of improvement; abrupt onset of high fever and severe respiratory distress (dyspnea, stridor, cyanosis), shock, death within 24–36 hours. Hemorrhagic meningitis can be present. [Note that direct skin contact with anthrax spores can result in **cutaneous anthrax** (11 confirmed or probable cases of cutaneous anthrax, in addition to 11 cases of inhalational anthrax, were associated with the 2001 anthrax attacks). In cutaneous anthrax, an area of local edema becomes a pruritic macule or papule, which progresses to a vesicle in 1-2 days, followed by an ulcer with subsequent development of a depressed black eschar within 7–10 days of the initial lesion. There is usually surrounding local edema, and small (1-3 mm) vesicles may surround the ulcer. The lesion is usually painless, but patients may also have fever, malaise, headache, lymphangitis, and painful regional lymphadenopathy.]

Pneumonic Plague. Fever, headache, weakness, and rapidly developing severe pneumonia with cough, chest pain, dyspnea, and tachypnea (particularly in young children). Cough can be productive of bloody, mucoid, or (less commonly) purulent sputum. Prominent gastrointestinal symptoms – including nausea, vomiting, diarrhea, and abdominal pain – may be present. Chest x-ray findings are variable but bilateral infiltrates

or consolidation is common; pleural effusions may be present. Massive mediastinal adenopathy occurs rarely. Complications include septicemia and meningitis.

Inhalational Tularemia. May see abrupt onset of fever, chills, malaise, headache, myalgias, joint pain, nonproductive cough, and progressive weakness. Persons with pneumonia can develop chest pain, dyspnea, bloody sputum, and respiratory failure. However, inhalational exposures can commonly result in an initial clinical picture of systemic illness without prominent signs of respiratory disease. The earliest chest x-ray findings may be peribronchial infiltrates, typically advancing to bronchopneumonia in >1 lobes, and often accompanied by pleural effusions and hilar lymphadenopathy – such signs may, however, be minimal or absent. Aerosol exposures to *Francisella tularensis* can incapacitate some persons in the first 1-2 days of illness, and pulmonary infection can sometimes rapidly progress to severe pneumonia, respiratory failure, and death. Although exposure to aerosolized *F. tularensis* is expected to principally cause primary pleuropneumonic infection, some exposures might contaminate the eye (resulting in ocular tularemia with conjunctivitis), penetrate broken skin (resulting in ulceroglandular or glandular disease), or cause oropharyngeal disease (with pharyngitis and cervical lymphadenitis).

_____ Mass Prophylaxis Clinic
For Dispensing of Antibiotics
Referral Form to Physician/Health Facility

Date: _____/_____/_____

Name: _____ DOB: _____/_____/____

Address: _____

Contact Number: _____

Referral Physician or Health Facility_____

Address: _____

The above named individual was seen at a mass prophylaxis point of dispensing site managed by the _____ for a possible exposure to anthrax. He/she is being referred to a physician for evaluation of the following symptoms:

- ☐ Cough
- ☐ Shortness of Breath
- ☐ Chest pain or discomfort on inspiration
- ☐ Bloody diarrhea
- ☐ Nausea and/or vomiting
- ☐ Fever / Chills
- ☐ Profound Sweating
- ☐ Muscle aches / Joint pain

☐ Other symptoms (specify)_____

The following prophylactic medication has been prescribed:

- ☐ Doxycycline 100mg PO q12 hrs X 10 days
- ☐ Doxycycline 100 mg PO q12 hrs X 20 days
- ☐ Doxycycline ____mg PO _____Dx _____days
- ☐ Ciprofloxacin 500 mg PO q12 hrs X 10 days
- ☐ Ciprofloxacin 500 mg PO q12hrs X 20 days
- ☐ Ciprofloxacin ____mg PO ____Dx ____ days
- ☐ **NO** antibiotic prescribed

If none prescribed:
☐ After evaluation, this individual should be started on a 10-day course of prophylactic antibiotic and will be notified if there is reason to continue beyond that time.

☐ This individual does not require prophylaxis.

_____ _____

☐ Pharmacist Signature Date
☐ Physician
☐ Nurse